

Needle-free Mesotherapy

Transdermal Electroporation



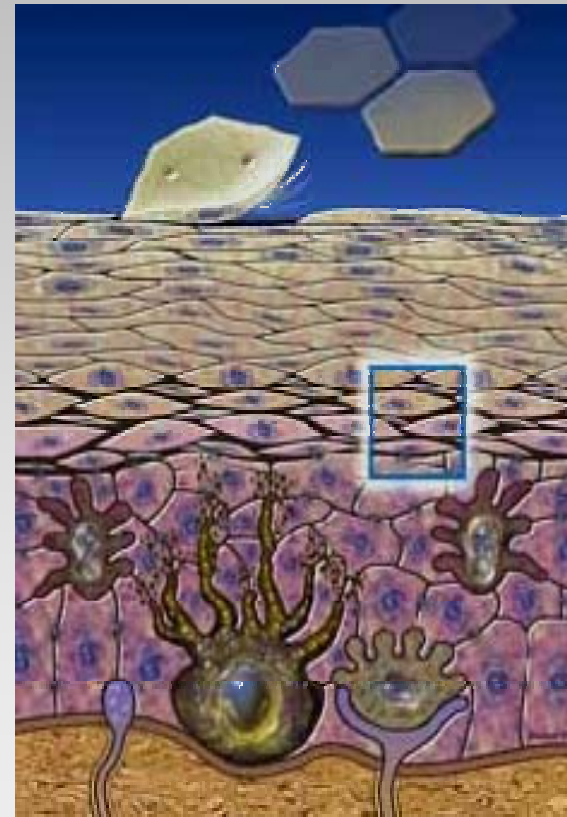
Skin

- One of the main functions of the skin is to act as a barrier protecting our body from the environment
- The skin is a natural barrier preventing the passage of exogenous substances into the body. These substances can be molecules or ions.
- The first and main obstacle is the stratum corneum (horny layer)

The passage of the substances

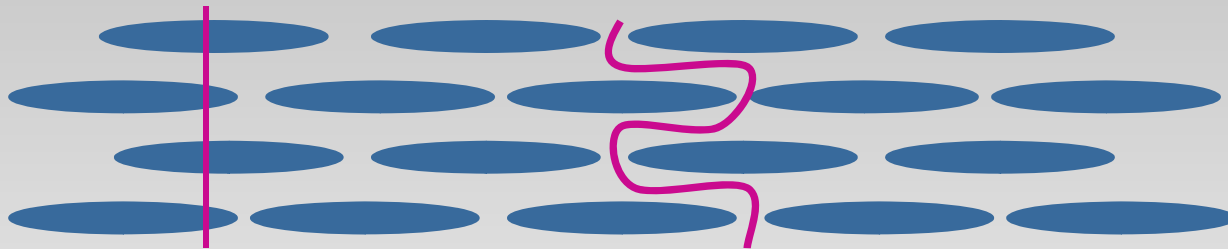
Requirements:

- cross the stratum corneum
- pass through the epidermis
- reach the dermis
- reach the subcutaneous tissue



Passage routes

- Transcellular route: Across the own cells by pores formed in cellular membranes (pathways)



- Paracellular route: Circulating through the intercellular space, crossing the lipids of the Pischinger's basal tissue

Properties of the substance

In order to penetrate through the skin, the substance has to be:

1. Dissolved, in case of being crystalline

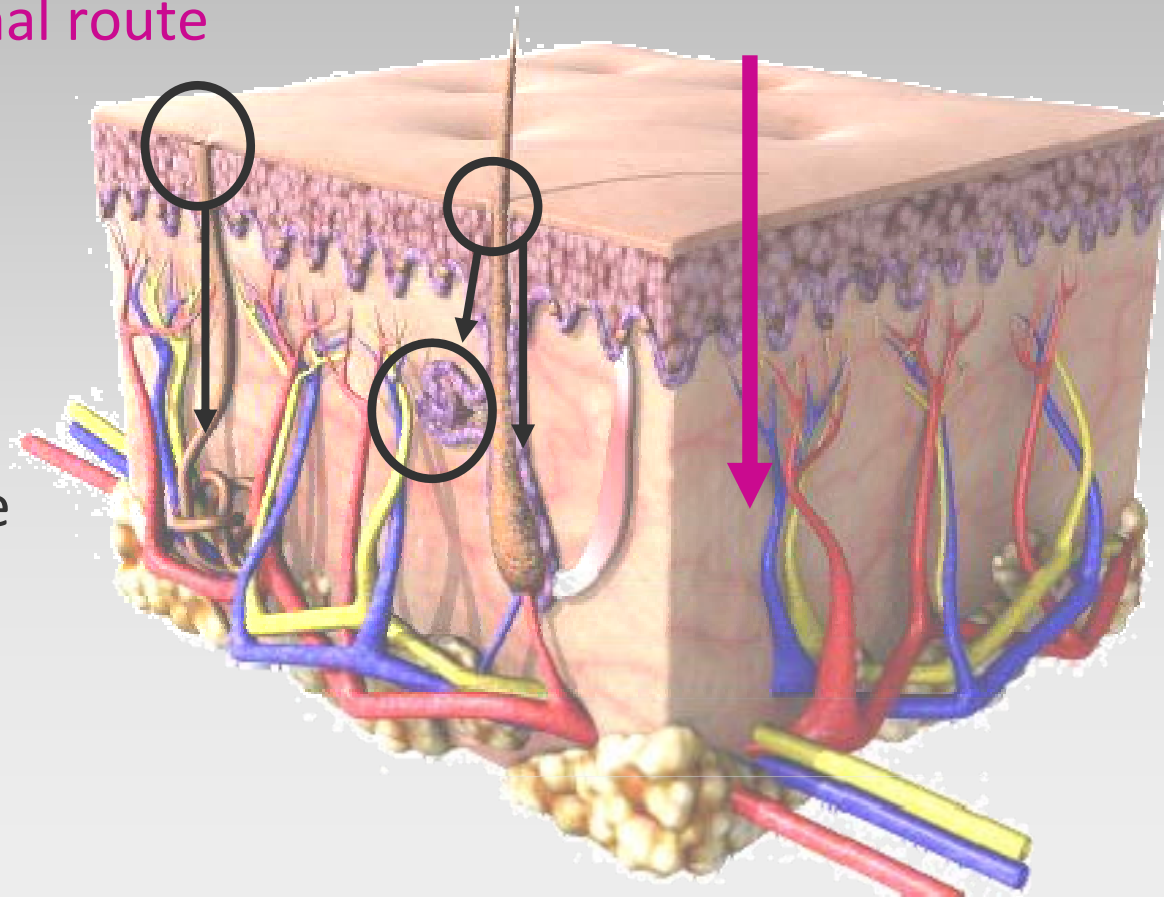
Penetration ways of a substance

- Complete absorption: When it reaches the cutaneous capillary microcirculation and is distributed through all the system.
- Fixation at the stratum corneum: It acts as a reservoir (“pool”) and has slow release into the capillaries of the dermis.
- Metabolic process: It is attributed to the presence of skin enzymes.

Transcutaneous penetration routes

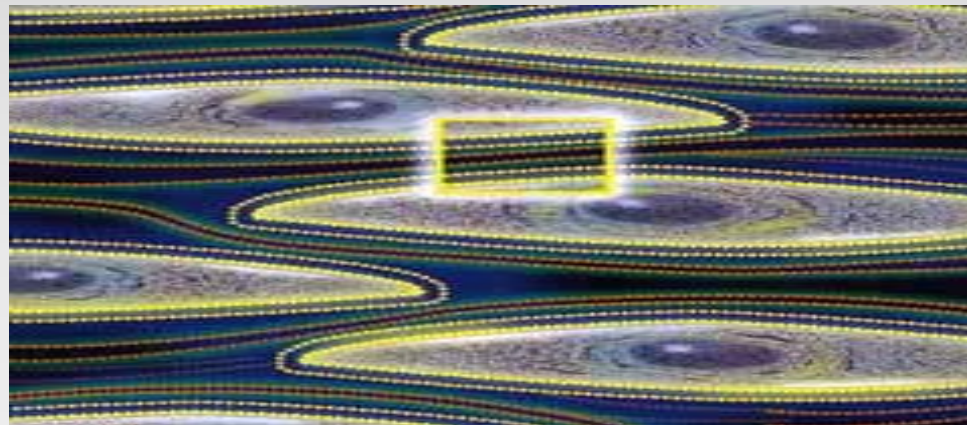
- Transepidermal route

- Anexial route



Transepidermal penetration route

- Transepidermal route: When a substance is crossing the skin overcoming the barrier of the horny layer. The stratum corneum is an heterogeneous structure composed of even and cross-linked queratinized corneocytes; the intercellular space is built from lipids.



Basic character of stratum corneum

- Lipophilic character.
- The resistance to the passage of a substance depends on its hydrophilic and hydrophobic properties.
- Thickness.
- Impermeability: The stratum corneum is 15 times less permeable to the passage of substances than the dermis. Its removal facilitates the product diffusion. Its moisturizing allows better penetration of substances.

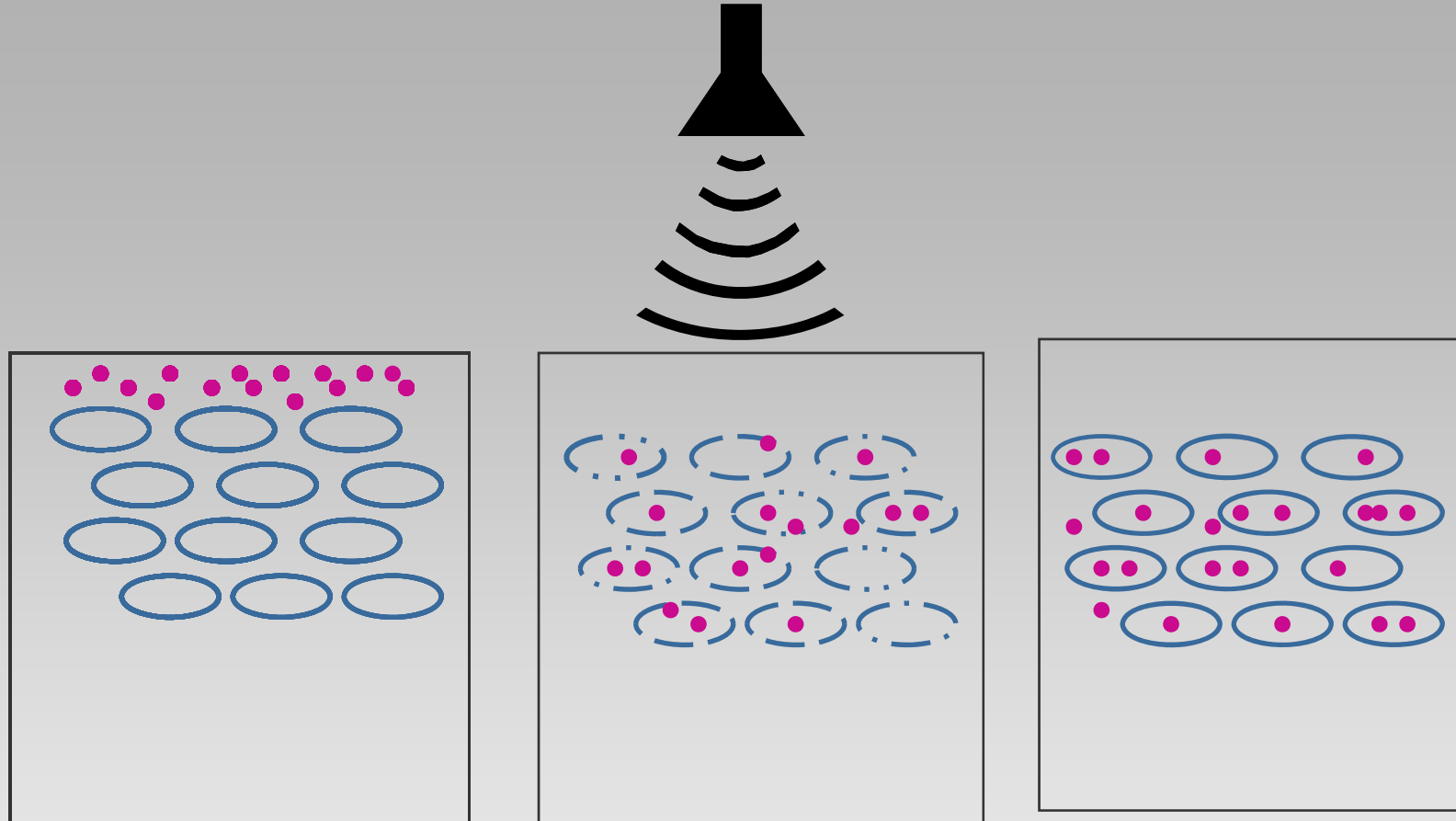
Anexial penetration route

- It is carried out by the sebaceous and sudoriparous gland
 - Pilosebaceous route: Absorption through the epithelial cells of the sebaceous gland. The products using it are non-ionic.
 - Sudoriparous route: This is used by ionic products.

Electroporation

- Defined by Lee in 1994 as a harmful aggression of the cellular membrane produced by means of electrical discharges of high voltage and pulses facilitating the pore formation (pathways) in the cell, and originating:
 - 1st cell lysis by electrochemical mechanism.
 - Increase of the permeability to the passage of substances into the interior of the cell.

- The electroporation is almost 40 years in existence. It is a physical method that uses short pulses of high voltage to make the cellular membrane permeable.
- This permeability is feasible for ions, antibodies, RNA and DNA, pharmaceutical substances, drugs, etc.
- Initially, it was used for the transfer of genes into mouse cells.
- In the decade of the 80's, the "in vitro" administration of the macromolecules into eucariotic cells was developed.
- In the 90's, it was used for in the administration of active principles by the transdermal route. Belehrader made the first clinical study on the use of the electroporation in the treatment of tumours with chemotherapy.
- This study was followed by the works of Heller, Mir, Gehl, Sersa, and many others.



The application of an electrical impulse temporally disorganizes the cellular membrane, permitting the entry of either DNA or a drug.

When the pulse ceases, the membrane recovers its structure and the substances penetrating into the interior of the cell are retained.

- The transepidermal transport will be performed by means of reversible electroporation.
- The equipment provides high frequency currents emitting electromagnetic waves (EMW) of hectometric modulated and pulsed frequency.
- The current (alternating current) of high frequency generates waves of high energy, but with the same characteristics as those of the receptor (cell).

E. Dubois Raimond's Law

- The reaction of excited tissues is determined by the Intensity of the operating current and the Pulse Growth Velocity.

The principles of the EMW

- When the electromagnetic waves (EMW) reach a cell, a difference of potential is established by the existing ionic charges between both media of the cellular membrane, i.e. interior and exterior media. This enables a redistribution by vibration at the same frequency, creating a conduction current generating an excitation of the cellular membrane.

- The membranes of these cells undergoing the effect of the EMW, change their physicochemical properties and modify the position of their transmembrane proteins and the system of the ion transport forming channels.

Alteration of the electroporated cellular membrane

- Alteration of the normal potential (- 90 mV), when the potential is between 240/330 mV, the pore size and its number increase, being this latter parameter determined by the conductance of the membrane.
- Process without modification of the temperature of the cellular membrane.
- The lipids of lipid bilayer undergo an electrorotation process forming a “pore” determined by the voltage.

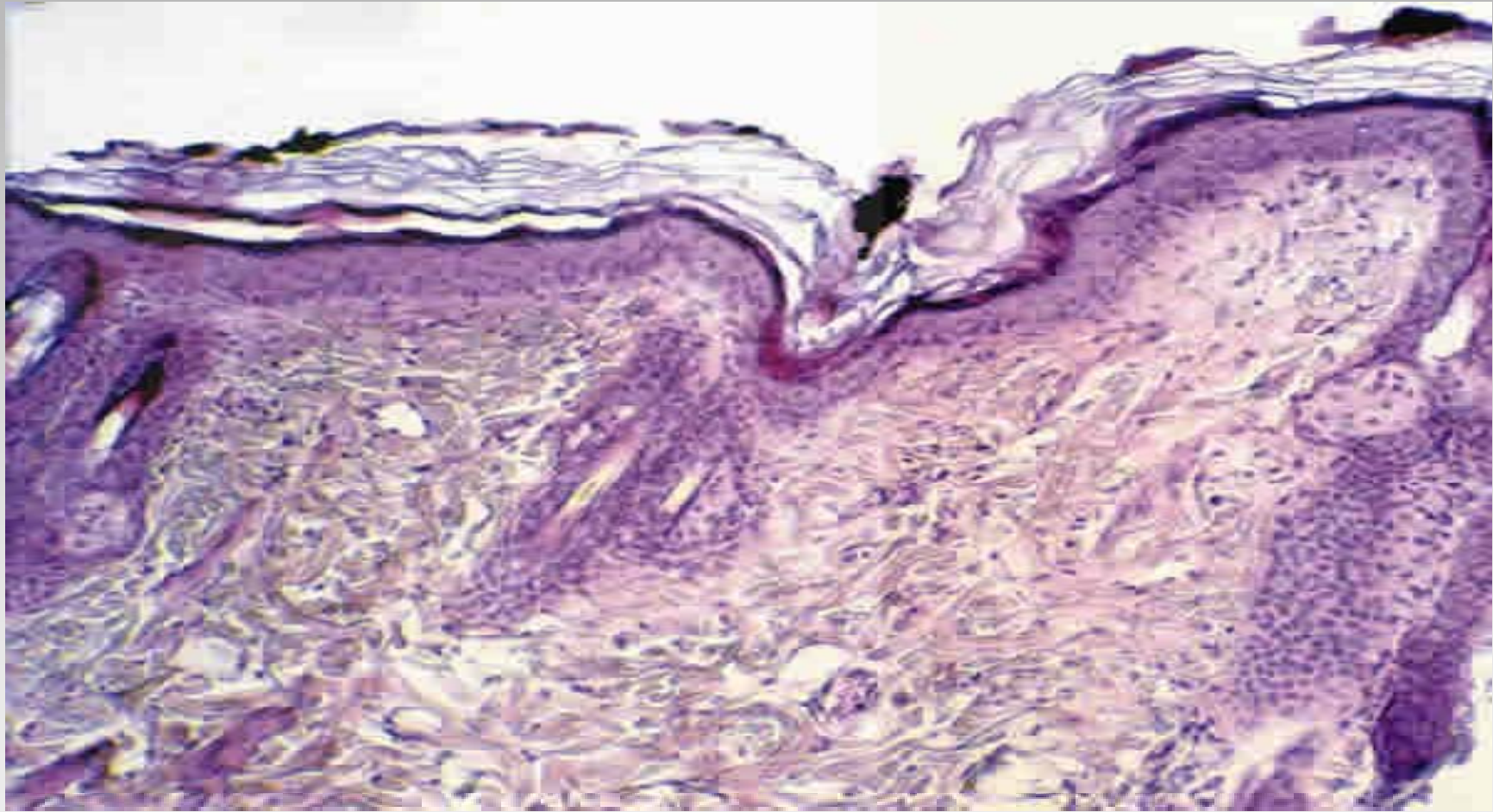
Reversible electroporation

- When the membrane potential is $< 1V$
- Non-maintained potential (Pulses)
- The cell undergoing this biological attack increases its permeability
- Integral recovery of the cell when its membrane potential is normalized. This is called On-Off mechanism

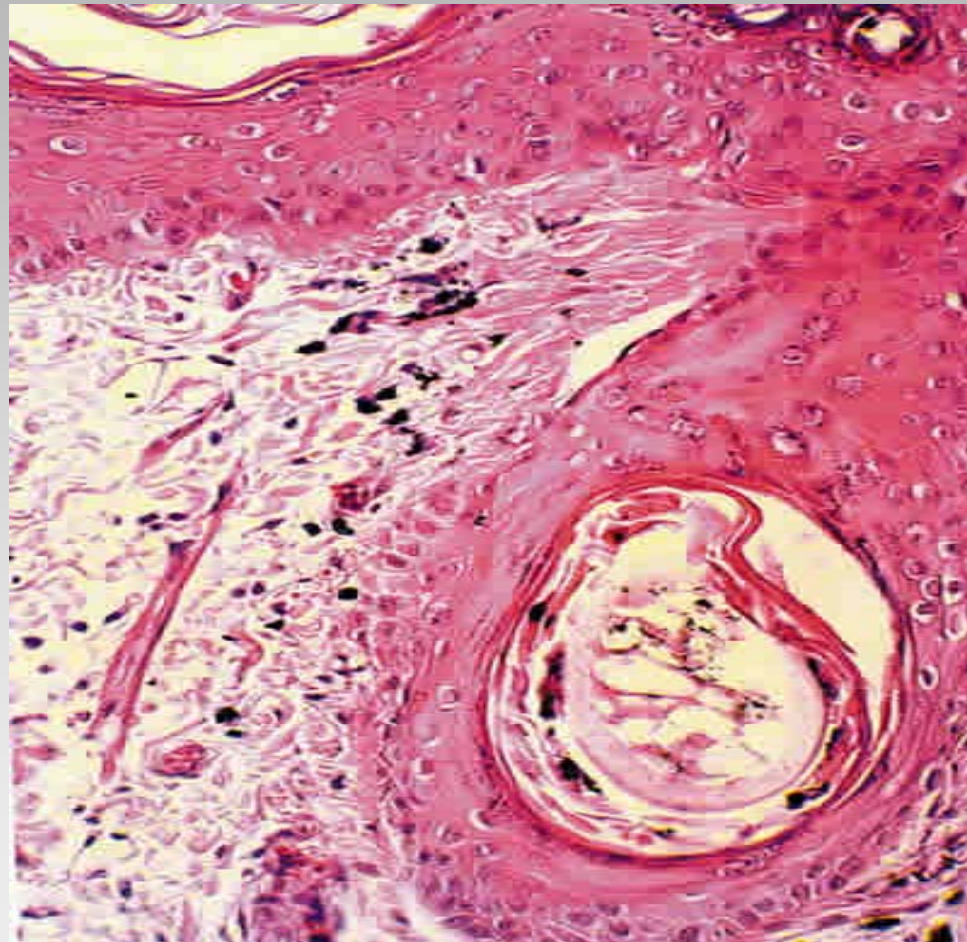
How does the electroporation work in the introduction of substances?

- Phenomena in the transcutaneous absorption.
 - In cellular membranes
 - In interstitial lipids (T-junctions)
- Phenomenon of electro-osmosis: the substances they penetrate through “pores” produced by the potential difference
- Phenomenon of passive diffusion
- The “passage” takes place during the electrical impulse
- According to Praunist, in 1999, the polarity of the substance does not matter
- The penetration velocity for hydrolipidic products is approximately 1 g /1 - 1,5 '

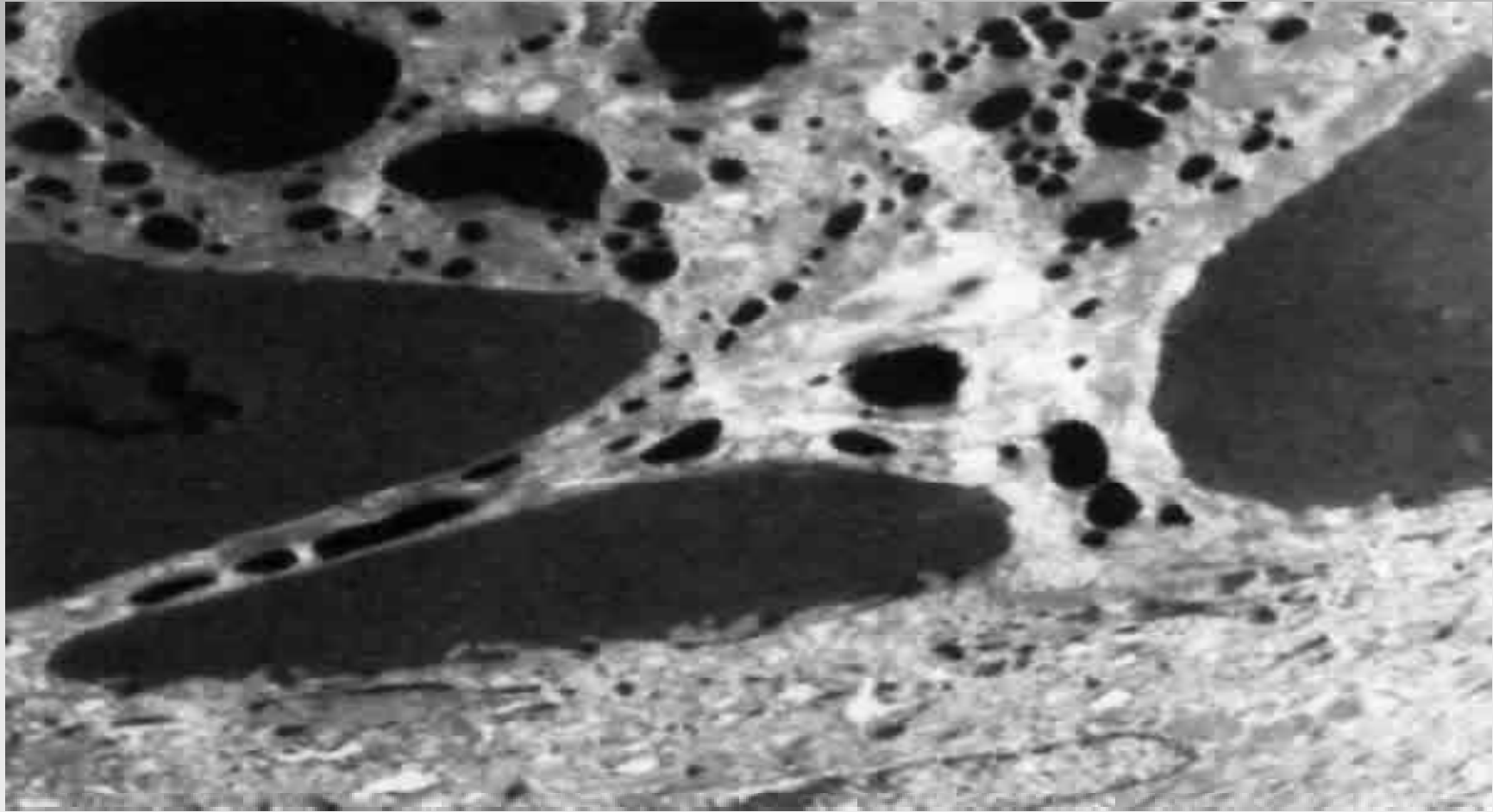
Chinese Ink particles (Biopsy)



24-h Biopsy



Channel opening



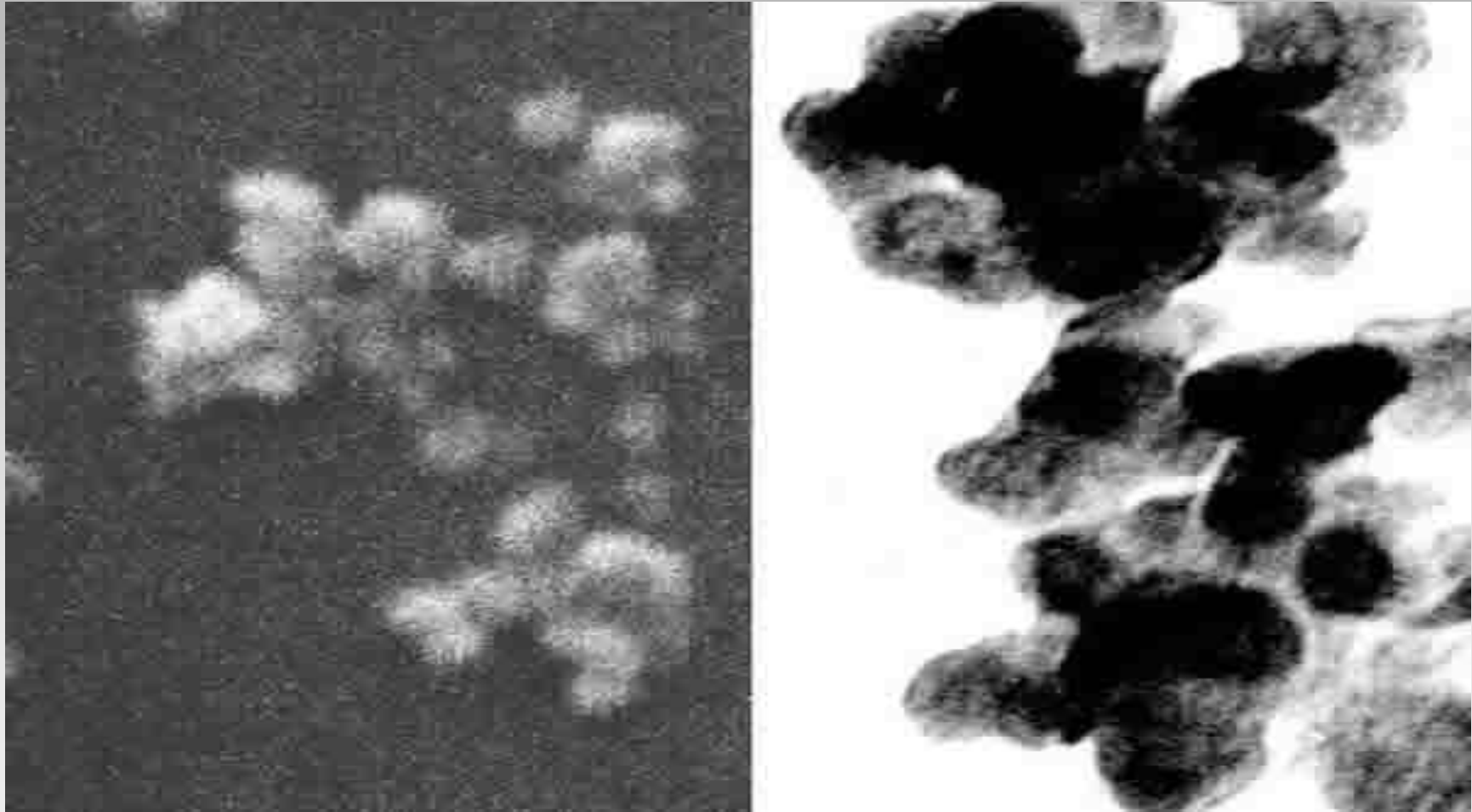
Intercellular communications



Cellular penetration



Comparative penetration



Physiological effects

- Reduction of the inflammation and oedema
- Time shortening of the haematoma reduction
- Increase of collagen and its orientation (Antiflaccidity effect)
- Possible application in acute processes without making tumefaction and oedema worse
- Penetration of transdermal products

MesoIn

- New electronic concept that generates and emits hectometric, pulsed and modulated EMW produced by high-voltage current.
- It does not warm up the cutaneous surface touching the electrode
- It does not have secondary effects
- It does not concern the electrochemical state of the substance

How does MesolN work?

- Reversible Electroporation
- It introduces molecules and macromolecules either ionic or non-ionic by means of the transdermal and anexial routes
- Contact of the test electrode with the skin allowing higher cellular resonance (piezoelectric cellular effect)
- There is no risk of chemical burns, the products do not ionise
- Permissivity to act in depth with low powers
- There is no wave refraction

Therapeutic indications

- Aesthetics:
 - Obesity and cellulites, flaccidity, cutaneous aging, scars, striae
- Transcutaneous product penetration:
 - Virtual syringe: reversible electroporation
- Alterations of the Locomotive Apparatus
 - Chronic and acute osteoarticular pathology, traumatism sequels and muscles breakage, fracture consolidation, neuralgias

Precautions of use

- Do not apply to patients with pacemaker
- Do not use in patients with epilepsy
- Do not use in pregnant women

Way of use

- Clean the zone to be treated with a peeling cleaner. Do not to use alcoholic or inflammable products
- Place the products to use, 2 to 5 ml according to the concentration and lipid content, into a syringe; apply by “dropping” into the zone to be treated. Approximate penetration time 1 -1,5’/ ml
- Select mode and power. Press “start” and slide the electrode.
- It is advisable during the session NOT to touch the patient, and to avoid the contact of the patient with metallic objects.