ROYAL STIMULATE

Poly-L-Lactic Acid

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ROYAL STIMULATE

Poly-L-Lactic Acid Injectable
Dermal Filler

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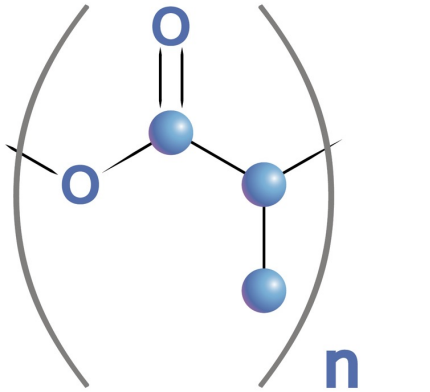
POLY-L-LACTIC ACID



Polylactic acid

Polylactic acid, is a synthetic polymer derived from natural sources such as maize, sugar beet or other starch-rich plants. The production process of PLLA involves the fermentation of plant raw materials into lactic acid, which is then polymerised to produce the final product.

Polylactic acid is a polymer, meaning that it consists of long chains of molecules of repeating monomeric units. The monomer in the case of PLLA is lactic acid. During polymerisation, lactic acid transforms into its dimeric forms (cyclic dimer - lactide) and then undergoes ring opening and polymerisation to form long polymer chains.

MECHANISM OF POLYLACTIC ACID ACTION

- **Injection and Placement:**

L-polylactic acid is injected subcutaneously in the form of microspheres suspended in sterile water for injection. These microspheres are designed to locate in the subcutaneous space and in the dermis, where they begin their function.

- **Inflammatory Response:**

Once injected, the body treats the PLA microspheres as foreign bodies. This triggers a localised, controlled inflammatory response, which is key to stimulating fibroblasts, the cells responsible for collagen production.

- **Polymer Hydrolysis:**

PLA is a biodegradable polymer that undergoes hydrolysis. This process involves the breakdown of the polymer by reaction with water present in the tissues. Hydrolysis leads to the gradual breakdown of PLA microspheres into lactic acid monomers.

MECHANISM OF POLYLACTIC ACID ACTION

- **Biodegradation and Resorption:**

Lactic acid, formed by hydrolysis of PLA, is naturally metabolised and eliminated by the body. During biodegradation, PLA stimulates fibroblasts to produce new collagen. The newly formed collagen replaces the gradually disappearing microspheres, leading to improved skin structure.

- **Stimulation of Collagen Production:**

The process of PLA biodegradation induces a local inflammatory response, which is a key factor in stimulating fibroblasts to produce type I and III collagen. Type I collagen is the main structural protein in the skin that provides strength and elasticity. Type III collagen is associated with wound healing and tissue regeneration.

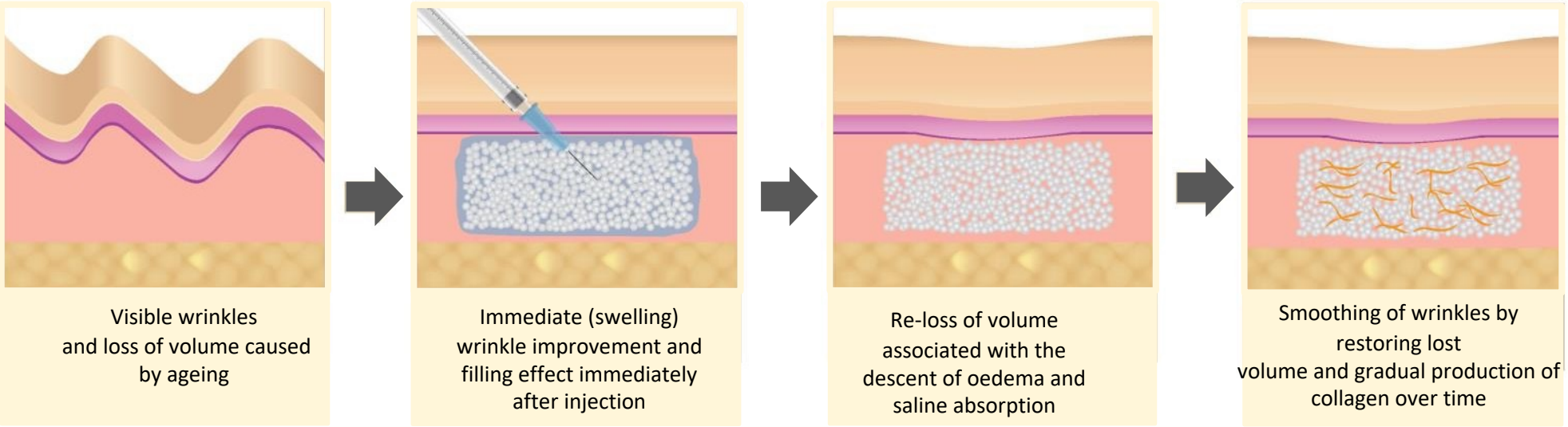
- **Long-term Effect:**

The effects of PLA injection are gradually visible. The initial filling effect is due to the presence of microspheres, which over time are replaced by newly formed collagen. This process lasts from a few months to a year, providing a long-lasting effect of rejuvenation and improved skin texture.

- **Degradation and Elimination:**

Eventually, all PLA degradation products are metabolised and eliminated from the body. This process is safe and leaves no permanent traces in the tissues.

MECHANISM OF POLYLACTIC ACID ACTION



Visible wrinkles and loss of volume caused by ageing

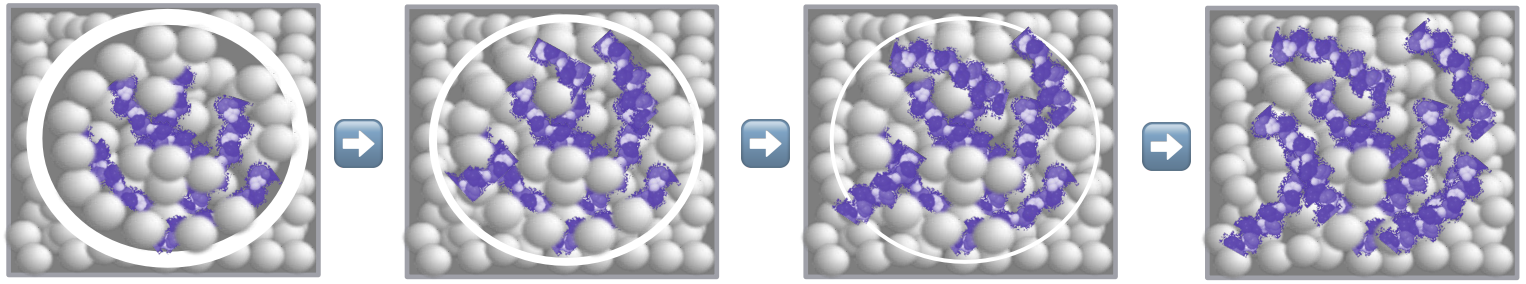
Immediate (swelling) wrinkle improvement and filling effect immediately after injection

Re-loss of volume associated with the descent of oedema and saline absorption

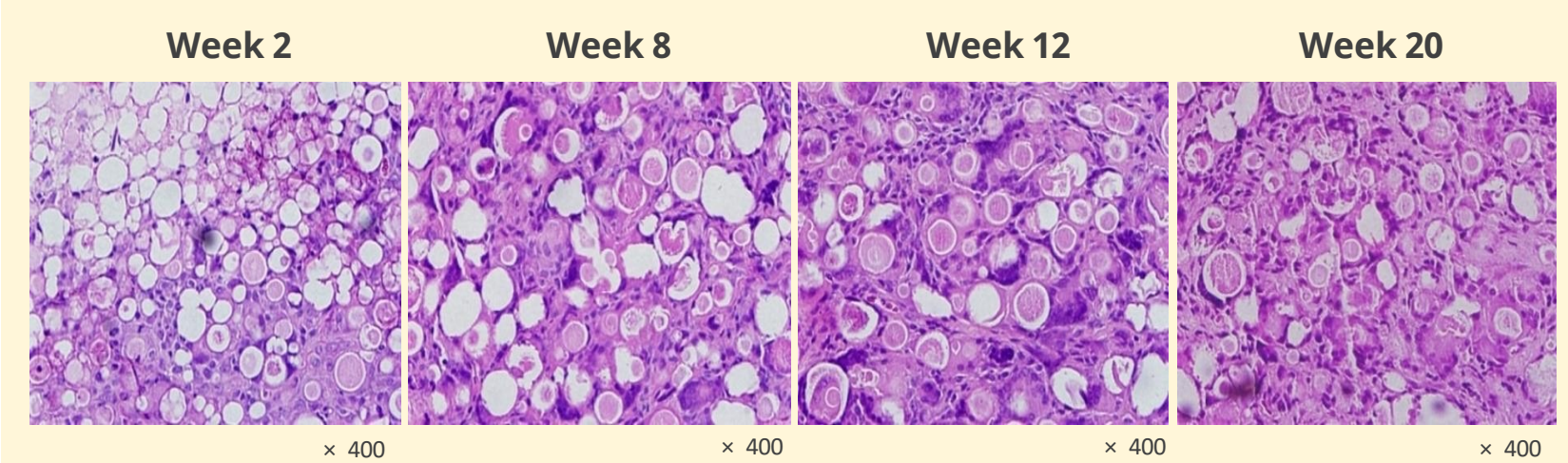
Smoothing of wrinkles by restoring lost volume and gradual production of collagen over time

In the 1st and 2nd week after injection, the corrected areas and volumes become visible again, but in the 4th to 8th week, the skin visibly thickens and remodels due to intensive cell stimulation. New collagen structures are formed over time as cells flow into the crystalline PLLA particles.

MECHANISM OF POLYLACTIC ACID ACTION



New tissue and collagen formation with cell influx between PLLA molecules



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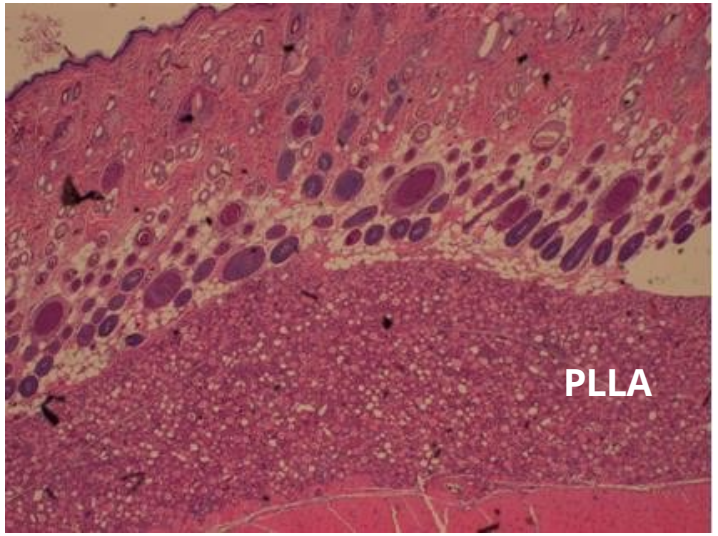
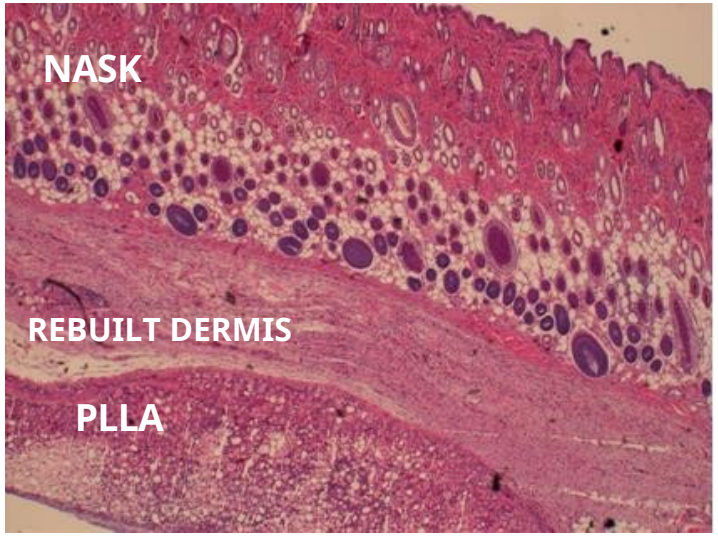
MECHANISM OF POLYLACTIC ACID ACTION

2 Weeks After Injection



4 Weeks After Injection



Once PLLA molecules have been injected into the dermis, the molecules remain in the same layer,
without moving to other tissues or areas,
as observed below at weeks 2 and 4 after injection.

PLLA METABOLISM

Hydrolysis:

PLLA is hydrolysed on contact with water and body fluids, leading to the formation of lactic acid. This process is catalysed by enzymes present in the body, such as esterases.

Inflammatory response:

When PLLA is introduced into the skin, the body may respond with a moderate inflammatory response, which is a normal healing process. Macrophages and other immune cells may participate in the breakdown of PLLA.

Resorption:

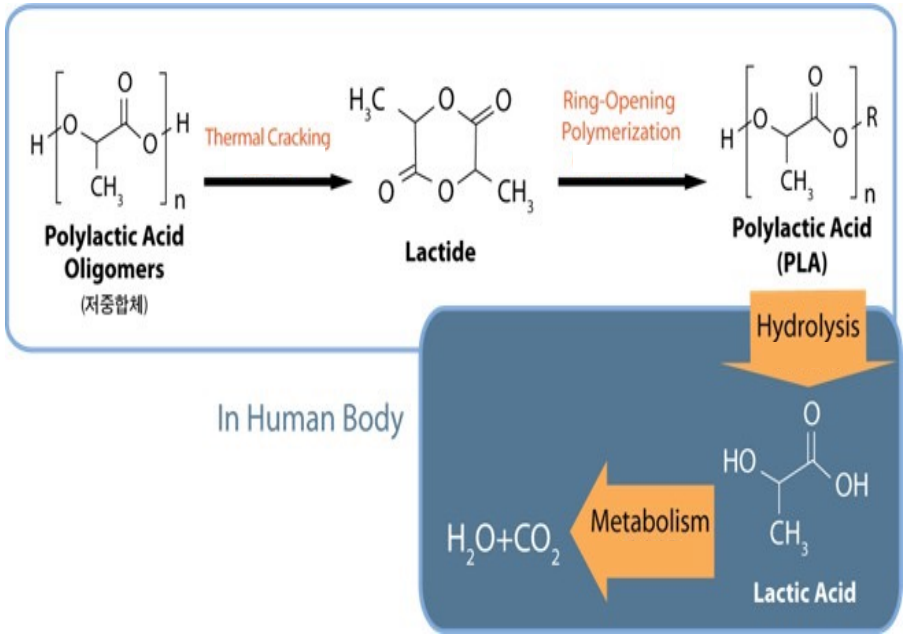
Lactic acid, a product of PLLA degradation, is naturally present in the body and is further degraded to water and carbon dioxide via the Krebs cycle (citric acid cycle) in the mitochondria of cells.

Elimination:

The final products of PLLA degradation, i.e. water and carbon dioxide, are eliminated from the body via the respiratory system (as CO2) and the urinary system (as water).

Cellular reactions:

The process of PLLA degradation can stimulate the synthesis of collagen and other extracellular matrix components by fibroblasts, which is used in aesthetic medicine to improve skin structure.



SPECIFIC PROPERTIES OF PLLA MICROSPHERES

- **Biocompatibility:**

PLLA is biocompatible, meaning that it does not cause toxic reactions in the body. This makes it safe for use in aesthetic medicine.

- **Biodegradability:**

PLLA degrades naturally in the body, eliminating the risk of permanent implants and enabling the skin's natural regenerative processes.

- **Controlled Resorption:**

PLLA's rate of biodegradation can be controlled by modifying its chemical structure and microsphere size, allowing the duration of action to be tailored to the patient's needs.

APPLICATION OF PLL IN AESTHETIC MEDICINE

L-polylactic acid has found wide application in aesthetic medicine, mainly as a biocompatible and biodegradable dermal filler. The main applications include:

- **Dermal fillers:** PLA is used to produce fillers that are injected under the skin to reduce wrinkles, restore facial volume and improve facial contours. It has a stimulating effect on collagen production, leading to a natural filling effect and skin rejuvenation.
- **Biodegradable lifting threads:** PLA is also used in the form of lifting threads, which are placed under the skin to mechanically lift sagging tissues and improve the facial oval. In addition to the mechanical effect, these threads stimulate collagen production, which has an additional rejuvenating effect.
- **Tissue regeneration:** Thanks to its biodegradable and biocompatible properties, PLA is used in regenerative medicine to produce scaffolds (scaffolds) for tissue engineering. These scaffolds promote tissue regeneration by providing a structure for new cells.

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FORMS OF POLYLACTIC ACID

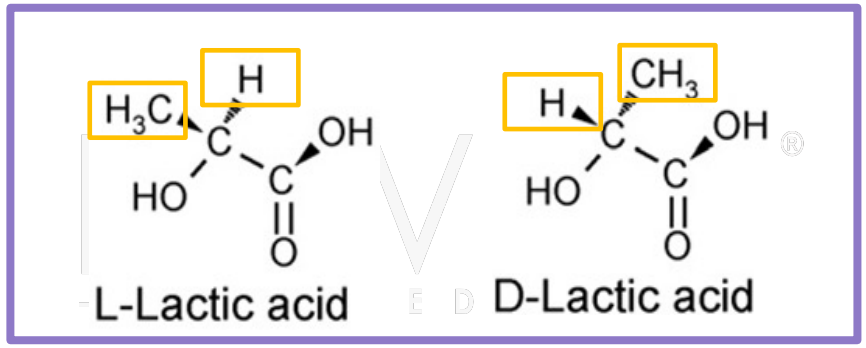
L-polylactic acid exists in two forms, L and D

Poly L- Lactic Acid - left-handed form - typically isolated from two racemates

Poly D- Lactic Acid - right-handed form

The lactic acid polymer consists of optical monomers, i.e. low molecular weight molecules.

The isomers, or right- and left-handed mirror images of the chiral molecule, have the same molecular formula but a different arrangement of atoms



DIFFERENCES BETWEEN L-PLLA AND R-PLLA ACID

L-PLLA	D-PLLA
It is biodegradable in a predictable and controlled manner. The degradation process of L-PLLA leads to the formation of lactic acid, which is metabolised by the body. This ensures that the degradation products are non-toxic and safely removed from the body.	Biodegradation of D-PLLA may be less predictable and the degradation products may not be as readily metabolised as with L-PLLA. This can lead to accumulation of degradation products, which is disadvantageous in medical applications.
More effectively stimulates the production of type I and III collagen. Type I collagen provides strength and elasticity to the skin, while type III collagen is associated with tissue regeneration.	It may not be as effective in stimulating collagen production as L-PLLA, making it less effective for aesthetic medicine applications.
The human body tolerates L-PLLA better because the L-isomeric form of lactic acid is naturally occurring in the human body. This biocompatibility means that L-PLLA causes fewer allergic and inflammatory reactions,	It is less biocompatible compared to L-PLLA. Although it can be used in certain applications, its tolerance by the human body is not as high, which can lead to a higher risk of adverse reactions.
Due to its higher crystallinity, L-PLLA has better mechanical properties. These properties are important in the context of dermal fillers and lifting threads, where durability and stability are key.	It is less crystalline, leading to poorer mechanical properties. This limits its use in contexts where higher strength standards are required.
It is widely used in aesthetic medicine. L-PLLA-based dermal fillers, such as ROYAL STIMULATE, are used to reduce wrinkles, restore facial volume and improve contours.	Less commonly used in aesthetic medicine due to inferior biocompatibility and mechanical properties.

BENCHMARKING ANALYSIS

	HA FILLER	CALCIUM FILLER	PLLA FILLER
COMPOSITION	Highly hydrophilic filler based on hyaluronic acid (a natural polysaccharide of biological origin).	Fine particles mineralised with calcium and water-soluble gel-based fillers.	A natural polymer produced from starch-rich plant substrates.
ADVANTAGES	Immediate effect. Benefits only mechanically filling skin lasting og 6 - 12 months.	It is used for deep wrinkles in middle-aged people. It is not extremely popular because it is difficult to remove and correct if the procedure is done incorrectly. It can result in nodules occurring in a thin layer.	A natural volumising effect that builds up over time with tissue remodelling and new collagen production. Physiologically improves the skin and does not mechanically stretch it.
DISADVANTAGES	Side effects: swelling , rejections due to cross-linking agents.	Inability to dissolve the filler in case of skin nodules, swelling, bruising or side effects.	No immediate change after treatment due to gradual effects over 2 years.
DURABILITY	6 – 12 months	12 months	**24 months**

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ROYAL STIMULATE is a suspension of L-polylactic acid molecules in injectable saline, which is injected subcutaneously or into deeper intradermal tissues where volume loss and fat atrophy have been identified.

1 vial contains:

150mg	Poly-L- Lactic
90mg	Sodium Carboxymethylcellulose
125mg	Mannitol

Medical device for injection

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INDICATIONS FOR ROYAL STIMULATE

- Compensation for Loss of Face Volume:
  fat atrophy
  sunken cheeks, flattened zygomatic area
  sunken temples
  deep nasolabial furrows
  irregular mandible outline
  skin flaccidity

- Reduction of wrinkles and fine lines
- Improving skin texture and elasticity
- Rejuvenation of specific areas: arms , décolleté, hands, body
- Restoration of correct facial geometry : PLLA can be used in reconstructive facial procedures, for example after trauma or surgery, to restore the natural shape and volume of the tissues.

6 UNIQUE FEATURES OF ROYAL STIMULATE

LONG-LASTING EFFECT

the improvement in skin tone appears gradually over several weeks, so that the positive changes in the face are associated with rest and relaxation, rather than with an aesthetic medical procedure

SAFETY

medical device for injection
medically certified

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LONG-LASTING EFFECT

the effects are visible for at least 25 months and can be permanently maintained with a maintenance treatment every 2 years

IMPROVING AND RESTORING OBJECTIVITY

The most powerful stimulator
thickens the skin and restores its defects
(wrinkles, folds, furrows)

RAPID CONVALESCENCE

The procedure does not require a large number of punctures,
slight bruising and swelling possible after the procedure

SHORT TREATMENT TIME

Treatment procedure
not exceeding 30 minutes

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TREATMENT PROTOCOL

PRODUCT ACTIVATION - add saline for injection slowly to the vial. Gently mix by rotating the ampoule up and down.

VORTEXING - place the ampoule in the Royal Stimulate Device shaker. Mix at 1000 rpm for 44 minutes.

USE - once mixing is complete, disinfect the rubber stopper of the vial with antiseptic and draw the appropriate amount of suspension from the vial using a sterile 18 G needle connected to a disposable sterile syringe, then secure the luer connector of the syringe with a combi topper.

The solution will be cloudy after mixing, but must be of homogeneous consistency. The prepared product must be injected within 72 hours of activation. If the product is not used within 72 hours, it must be disposed of.

TREATMENT - During treatment, use a sterile 26 G cannula or a sterile 26/27 G needle, depending on the individual treatment objective. Administer the product evenly, retrograde - linear, fan-shaped in areas with firmness loss and lipodystrophy.

MASSAGE - After completing the injection , disinfect the skin and perform an intensive massage of the treatment area.

POST-TREATMENT RECOMMENDATIONS !!! - After the treatment, instruct the patient on the necessary post-treatment procedure. Failure to comply with the recommendations may result in the appearance of secondary complications.

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DILUTION PROTOCOL

Amount of activator (injection saline) used :

6ml -8ml - SAFE DILUTION:

for working on large areas
for people with high elastosis, flabby skin, little fat padding

4ml -4.5ml - DILUTION FOR ADVANCED

for volumetric effects
for dense, hard skins with localised dysmorphic tissue, lower dilution

An optional anaesthetic should be included in the dilution,
the volume of which must be subtracted from the volume of the activator

POST-TREATMENT

- **Massaging the injection area:**

After treatment, the areas in which PLLA has been injected should be massaged vigorously. It is recommended to massage for 5 minutes, 5 times a day for the first 5 days after treatment. Massaging helps to distribute the product evenly and prevents the formation of lumps. 5 - 5 - 5

- **Cooling the injection site:**

Applying cold compresses for 15 minutes every hour for the first 24 hours can help reduce swelling and redness.
In addition to the recommended massages, avoid touching the injection site to reduce the risk of infection.

- **Avoiding exercise:**

It is recommended to avoid strenuous physical activity, exertion and exercise for at least 24-48 hours after treatment to minimise the risk of increased swelling and bruising.

- **Avoidance of extreme temperatures:**

For at least one week after surgery, patients should avoid exposure to extreme temperatures such as saunas, steam rooms, hot baths or intense cold.

- **Protection from the sun:**

It is recommended to avoid direct exposure to the sun and tanning beds for at least two weeks after treatment. Use creams with a high SPF to protect the skin from UV radiation.

- **Use of gentle cosmetics:**

Aggressive cosmetic treatments such as chemical peels, microdermabrasion or lasers should be avoided for the first few days after treatment.

IMPORTANT INDICATIONS:

1. Use the product for moderate corrections only. Any excessive corrections or injections are not permitted. Do not apply into the redness of the lips.
2. Only inject the product into the lower layers of the dermis or layers of subcutaneous tissue.
3. Patients generally experience swelling at the injection site (up to 30 minutes). For this reason, it may appear that the skin at the treatment site has completely filled in.
4. Patients should be advised that the swelling will subside within a few hours to a few days after the procedure, which may result in the reappearance of the primary skin defect.
5. In the initial phase after the procedure, the original folds and wrinkles may still be visible. The expected end result of the treatment occurs when the product has fully remodelled the tissues. The final result should be assessed after a few weeks. If the result of the treatment is unsatisfactory, a repeat treatment should be considered.
6. Do not inject the product to a shallow depth, closer to the outer layer of skin to prevent lumps or bumps at the injection site.
7. Injection of the product into the lumen of a blood vessel may cause complete or partial obstruction of the vessel, which may result in skin necrosis.
8. Typically, 2-3 treatment sessions are used at intervals of 4 to 8 weeks.
9. The product is visible on ultrasound and magnetic resonance imaging, but is not visible on CT or radiography.

ROYAL STIMULATE DEVICE

Compact device used for rapid and efficient mixing of ampoules and small liquid samples. It works on the principle of creating a vortex inside a closed ampoule or vial, which is placed on the device's rubber head and vibrated. The intense vortexing movements allow the ingredients to be thoroughly mixed, even those with very different properties, ensuring the precise combination of substances and the homogeneity of the solution.

The device is essential for the correct preparation of the Royal Stimulate volumetric stimulator.

Mix at 1000 rpm for 44 minutes

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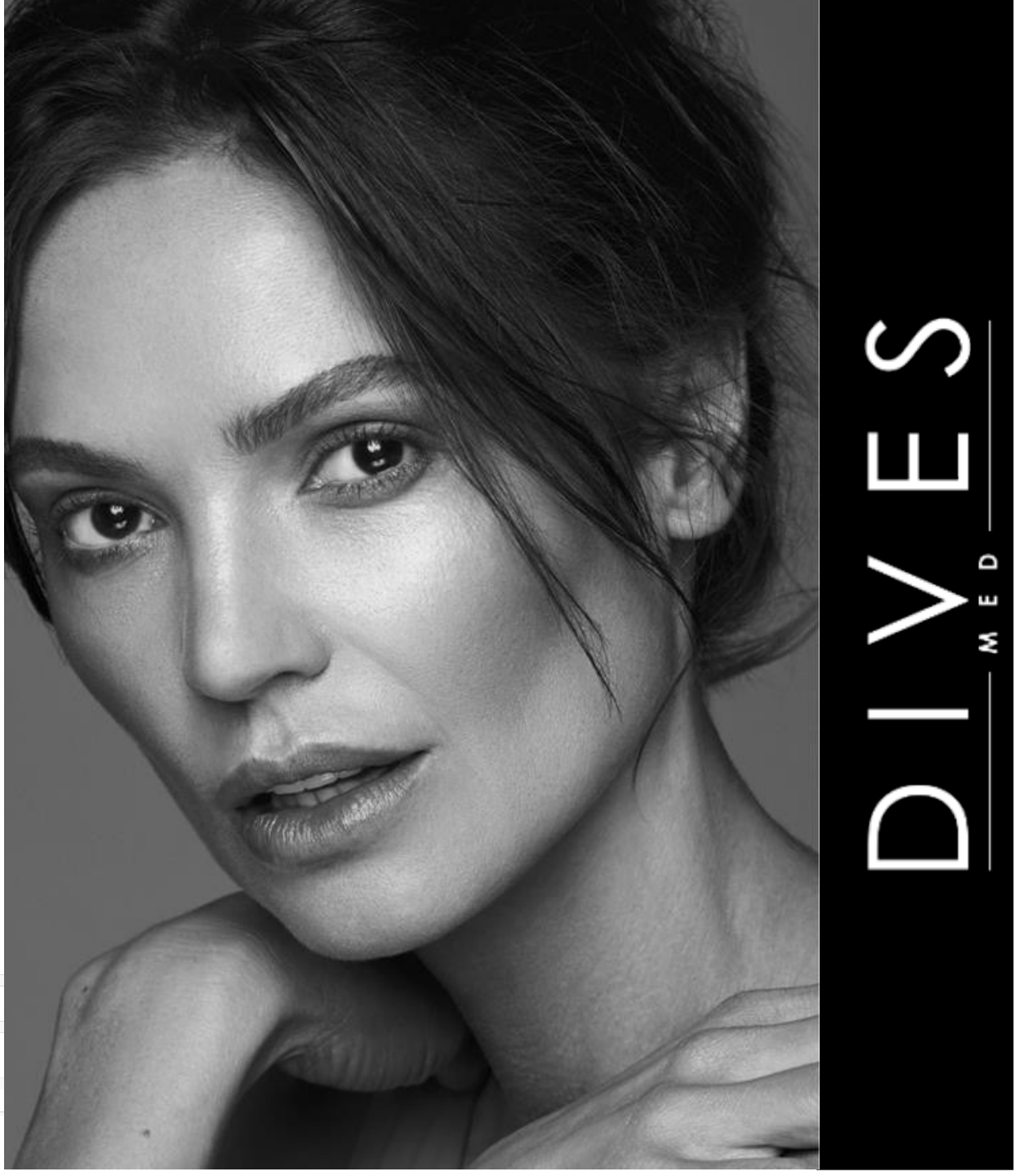
CONTRAINDICATIONS

- pregnancy or breastfeeding
- cancer
- bacterial, viral, fungal disease
- skin infection at the treatment site
- active inflammation
- fever
- autoimmune diseases
- blood clotting disorders
- Hydroxyapatite in the treatment site



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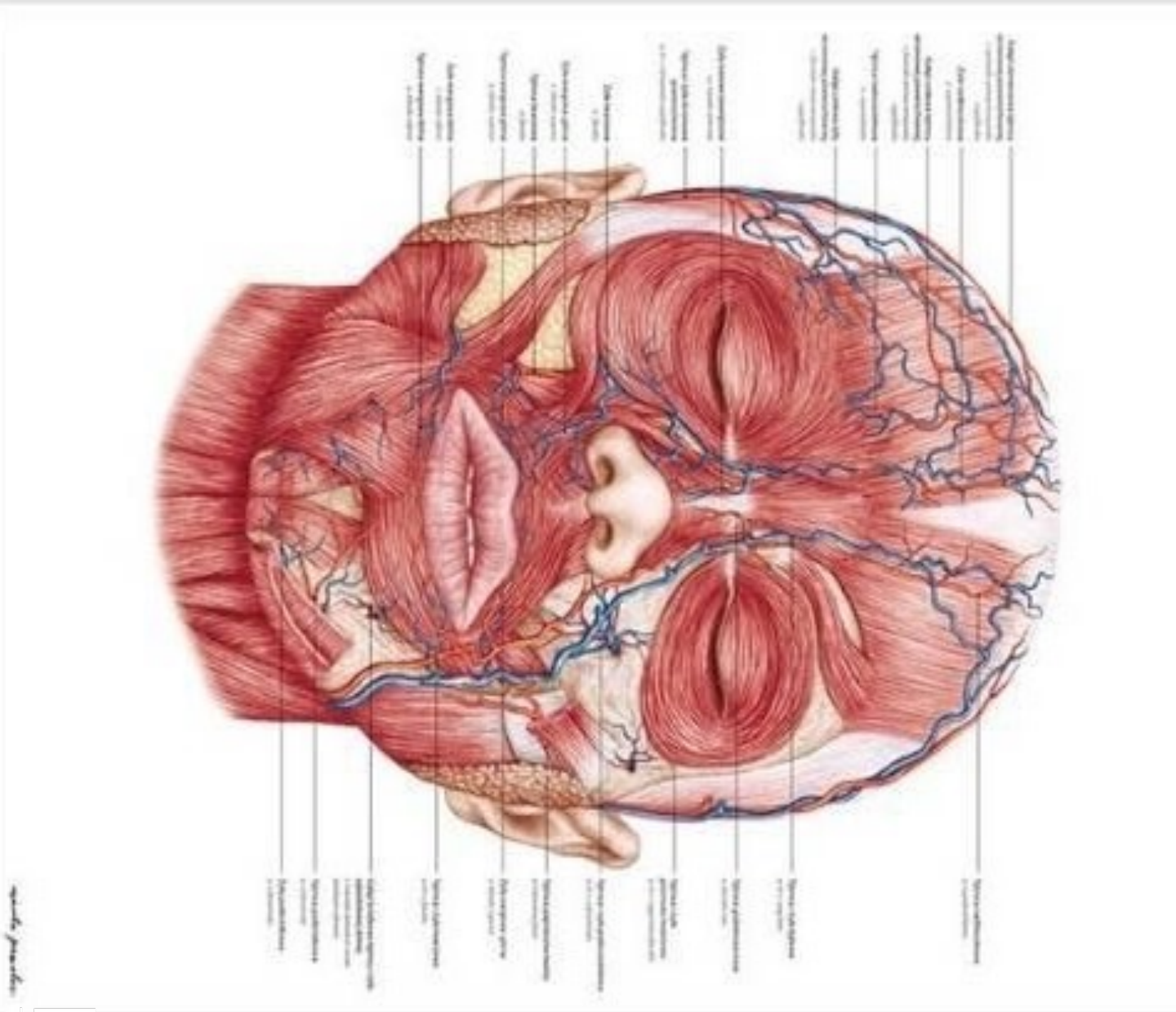
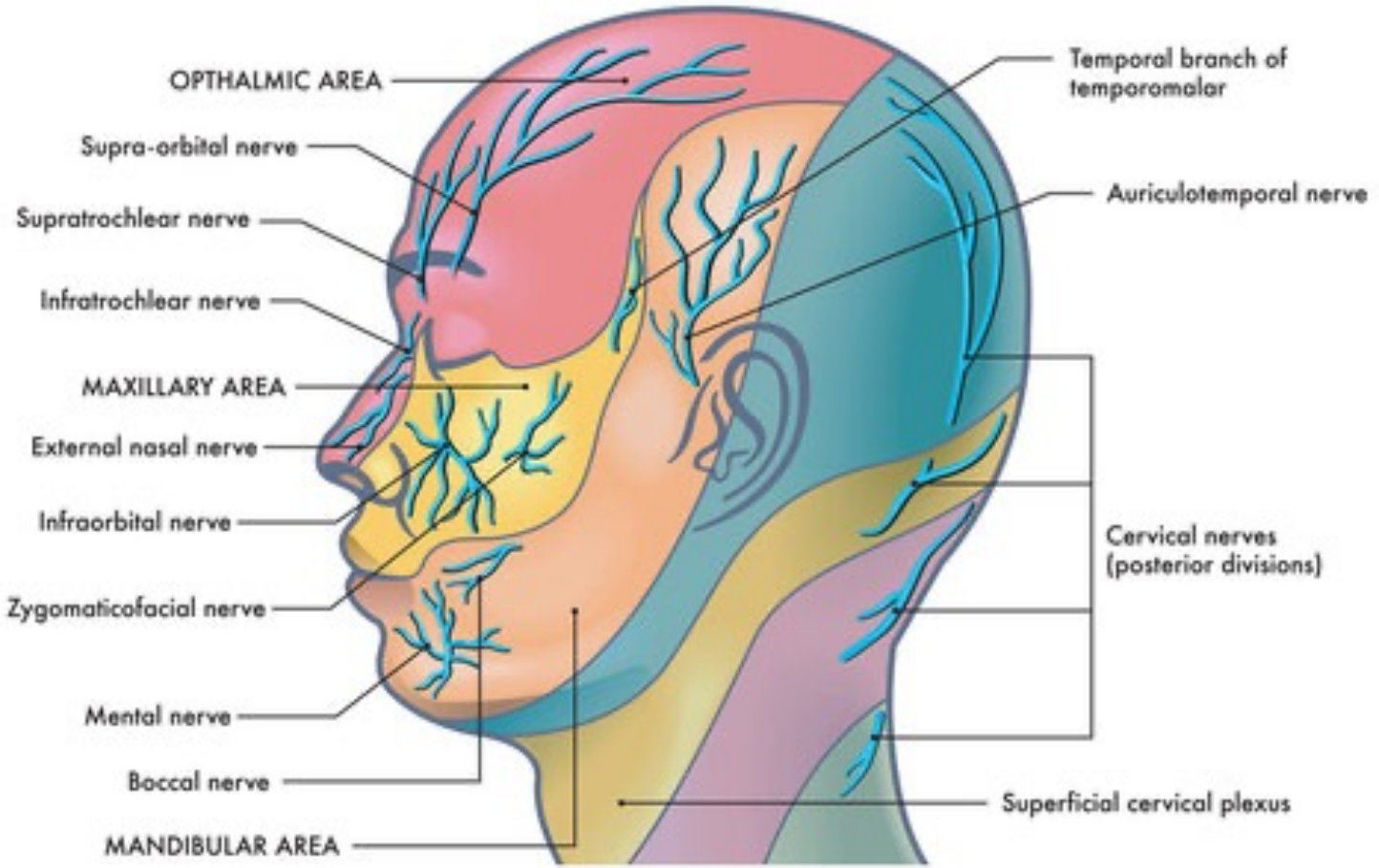
FACIAL VASCULARISATION



NERVE SYSTEM



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COMPLICATIONS

- Inflammatory reactions (swelling, redness)
- Swelling of varying intensity , lasting up to a week
- Subcutaneous papules: May appear as hard, palpable lumps under the skin. They are usually the result of improper injection technique or excessive amounts of product administered in one place.
- Inflammatory nodules: Are more painful and may be visible on the surface of the skin. Inflammatory nodules may require treatment, such as steroid injections or surgical intervention.
- Asymmetry: Uneven distribution of PLLA can lead to facial asymmetry. This can be caused by improper injection technique or and too much product administration
- Skin overcrowding effect - This can be caused by incorrect injection technique or and too much product administration
- Calcifications: Long-term presence of PLLA in tissues can lead to the formation of calcifications, which are hard mineral deposits that can be felt under the skin.
- Material migration: PLLA can migrate from the injection site, leading to unsightly effects
- Hypersensitivity reactions: In extremely rare cases, patients may experience allergic reactions to PLLA, manifesting as itching, hives or rashes.
- Vascular obstruction: Injection of the product into the lumen of a blood vessel may cause complete or partial obstruction of the vessel, which may result in skin necrosis.

PLLA A CaHA

- Biochemical interaction: polylactic acid is degraded in the body, leading to the formation of lactic acid. In an environment where calcium hydroxyapatite is already present, PLLA degradation products can react with CaHA, which can trigger an intense inflammatory response.

- Risk of Calcification: The degradation of PLLA in the presence of CaHA can lead to the formation of calcium deposits, which can trigger local inflammation and the formation of calcifications. Calcifications can cause hardening and heterogeneity of the tissue, which is undesirable in aesthetic medicine.

- Chemical Interactions: Calcium hydroxyapatite chemically reacts with PLLA causing the formation of subcutaneous calcifications. The degradation products of both materials can react with each other, leading to unpredictable chemical effects that can aggravate the skin and subcutaneous tissue.

- Tissue infections: Mixing two different biomedical materials can create an environment conducive to the growth of microorganisms. A microenvironment with the presence of both PLLA and CaHA may increase the risk of infection, as degradation products may affect immune function at the injection site.

THANK YOU!