AGEX*fill*

AGEX DERMAL FILLERS USER GUIDE

With the collaboration of
Dr Enrico Massidda, Cosmetic Physician

AGEX
by PHARCOS

PROTOCOLS AND TECHNIQUES BY DR. ENRICO MASSIDDA

This Guide, which would not have been possible without the invaluable contribution of Dr Enrico Massidda, a Cosmetic Physician with extensive experience in the field of dermal fillers, aims to provide the practitioner with all the support necessary to optimise the use of the product, Agex Fill.

Dr Massidda has developed protocols and techniques that maximise the product's performance, guaranteeing efficacious and natural results from the very first treatment.

Based on his or her experience, the practitioner will select which protocols and techniques to use, and may even decide to combine them if they see fit.

AGEX *fill*

CROSS-LINKED VOLUMISING HA + FREE BIO-STIMULATING

Agex Fill is a range of dermal fillers designed to correct both minor imperfections and deeper blemishes. The range consists of three fillers of differing filling power, which exert tissue bio-stimulation activity and a long-term restructuring effect.

HA at differing molecular weights: cross-linked + 5-10% linear or free, slow-release

1. **VOLUME**: Reduces volume physiologically
   - Integrates immediately into tissues
   - Homogeneous distribution
   - Natural results

2. **STRUCTURE**: Improves tissue and stimulates receptors
   - Stimulates the CD44 receptor
   - Promotes the proliferation of fibroblasts and basal cells in the epidermis
   - Promotes neoangiogenesis and collagen production

3. **HYDRATION**: Restores the natural osmotic concentration of tissues
   - Draws in and retains up to 1000 times its weight in water

AGEX

CROSSLINKING	VOLUME	BIOSTIMULATION
◆◆◇◇◇	●○○○○	●●●●●

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CROSSLINKING	VOLUME	BIOSTIMULATION
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AGEX fill

CROSSLINKING	VOLUME	BIOSTIMULATION
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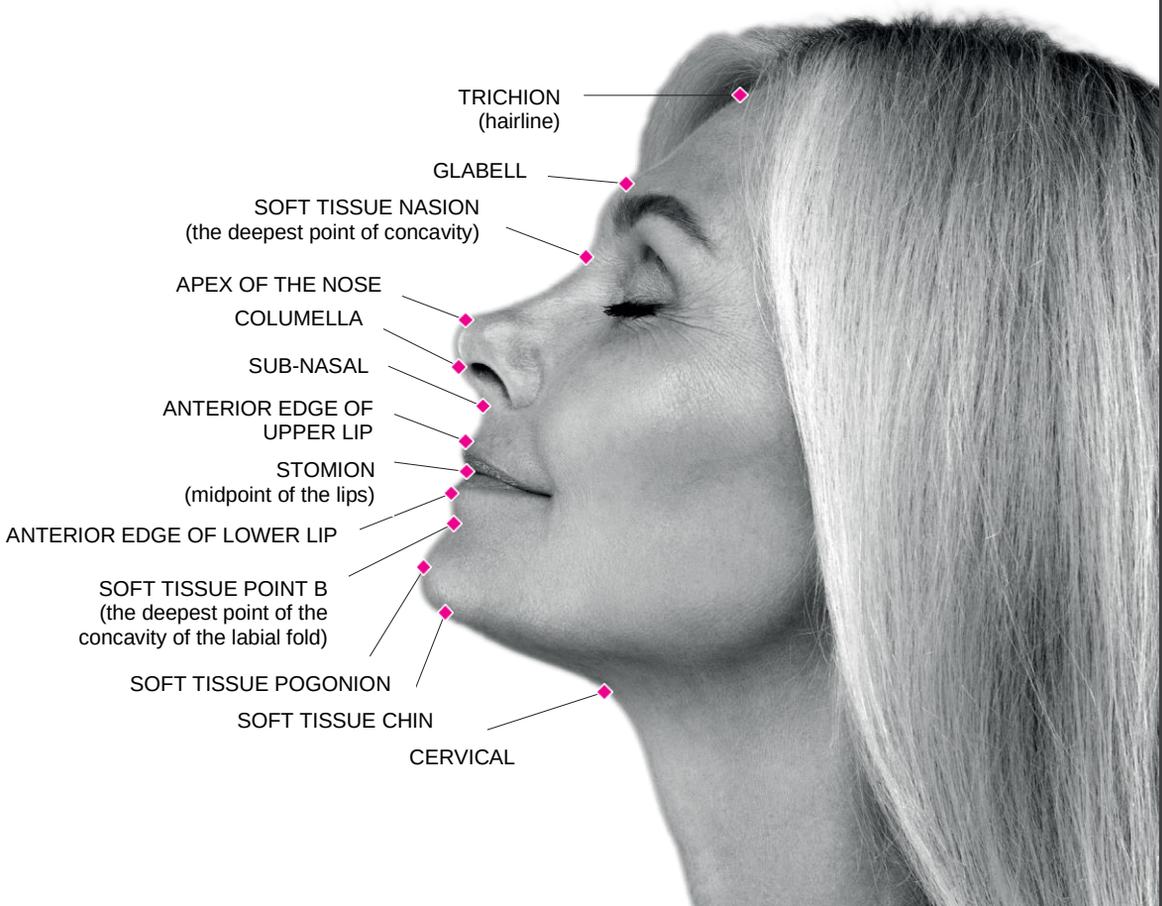
1. AGEING AND FACIAL ANATOMY

Time inevitably exerts a transformative action on the face, the effects of which may vary considerably from one subject to another. The timing of these changes may also vary depending on several factors.

However, there are some characteristics that are common to all mature faces. These points also act as indicators that help to gauge the current state of the various areas of the face and the type/scope of treatment required:

- Inversion of the Triangle of Youth
- Irregular skin surface (folds, rough patches, wrinkles)
- Skin pigmentation disorders (dark circles, superficial capillaries, other pigmentary conditions)
- Loss of proportion of the skin envelope (loss of subcutaneous fat, sagging of soft tissue)
- Glabellar lines
- Drooping eyelids (ptosis)
- Sunken eyes (supraorbital hollowness)
- Wrinkles around the eyes
- Infraorbital hollowing (bags under the eyes)
- Atrophy of the fat in the upper cheeks (malar fat pad)
- Deep nasolabial folds
- Wrinkles around the mouth
- Loss of lip volume and perioral wrinkles
- Drooping mouth corners and cheeks (puppet lines)
- Wrinkles under the lips (sublabial fold)
- Irregular and 'drooping' chin contour



2. PRODUCTION PROCESS AND TECHNICAL SPECIFICATIONS

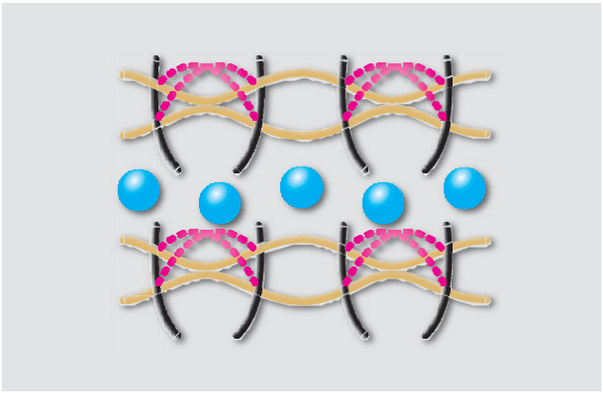
AGEX fill

IALOBILAYER TECH

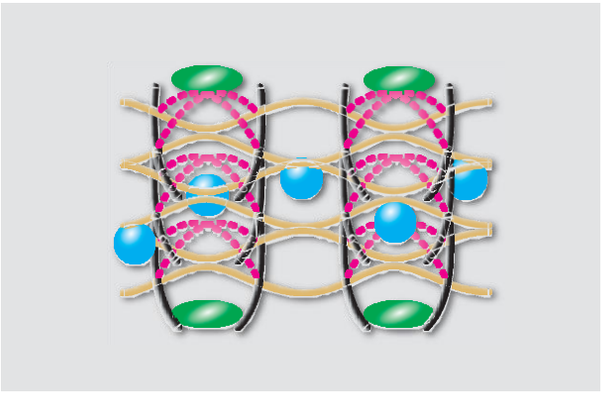
TECHNOLOGY THAT COMBINES CROSS-LINKED FILLER HA WITH FREE BIO-STIMULATING HA

AGEX FILL is excellent for repairing specific imperfections, while also providing natural correction for wrinkles and volumes and restoring skin firmness and tone. This is possible thanks to the innovative

IALOBILAYER® technology, which uses cross-linked hyaluronic acid (HA) at differing molecular weights, alternating with non-cross-linked hyaluronic acid, at varying percentages depending on the type of product. The hyaluronic acid used is an uncut monophasic gel with 1-2 micron particles; this results in a more homogeneous gel and better distribution in the tissues. Studies have demonstrated the effectiveness of this technology in stimulating the proliferation of fibroblasts in the human dermis, resulting in increased production of collagen and elastin.



Alternating layers of cross-linked and free native HA



The free HA is protected against enzymatic degeneration and released gradually

2.1. PRODUCTION PROCESS

IALOBILAYER®-TECH uses a very pure pharmaceutical-grade sodium hyaluronate, produced by bacterial fermentation, which is mixed slowly at low temperature and purified by dialysis for 24 hours, resulting in the so-called 'soft-crosslinking':

- Evaluating the degree of cross-linking
- Purification with WFI
- Minimal use of BDDE
- Low residual BDDE (lower than fillers having the same viscosity)
- Low risk of side effects and preservation of skin health
- Prevention of hyaluronic acid degradation

2.2. MAIN ADVANTAGES

- Cross-linked filling HA + free biostimulant HA, protected and slow-release
- Raw materials comply with the highest quality standards
- Minimum BDDE levels
- High HA concentration

3. AGEX*fill*

Skin Booster with bio-restructuring effect for complete skin rejuvenation. It restores elasticity and hydration, and stimulates tissue regeneration.

CHARACTERISTICS

- Biological receptive stimulation activity (tissue redensification)
- Elasticity
- Softness and flexibility
- Receptive stimulation

SUPPLIED WITH

- 27 G x 37 mm cannula
- 26 G x 13 mm guide needle

COMPATIBLE WITH

- 30 G x 13 mm needle
- 30 G x 4 mm needle

PACKAGE CONTAINS 3 pre-filled disposable syringes

DOSAGE 1.1 ml

COMPOSITION Cross-linked and linear hyaluronic acid (with Hyalobilayer® technology)

CONCENTRATION 25 mg/ml

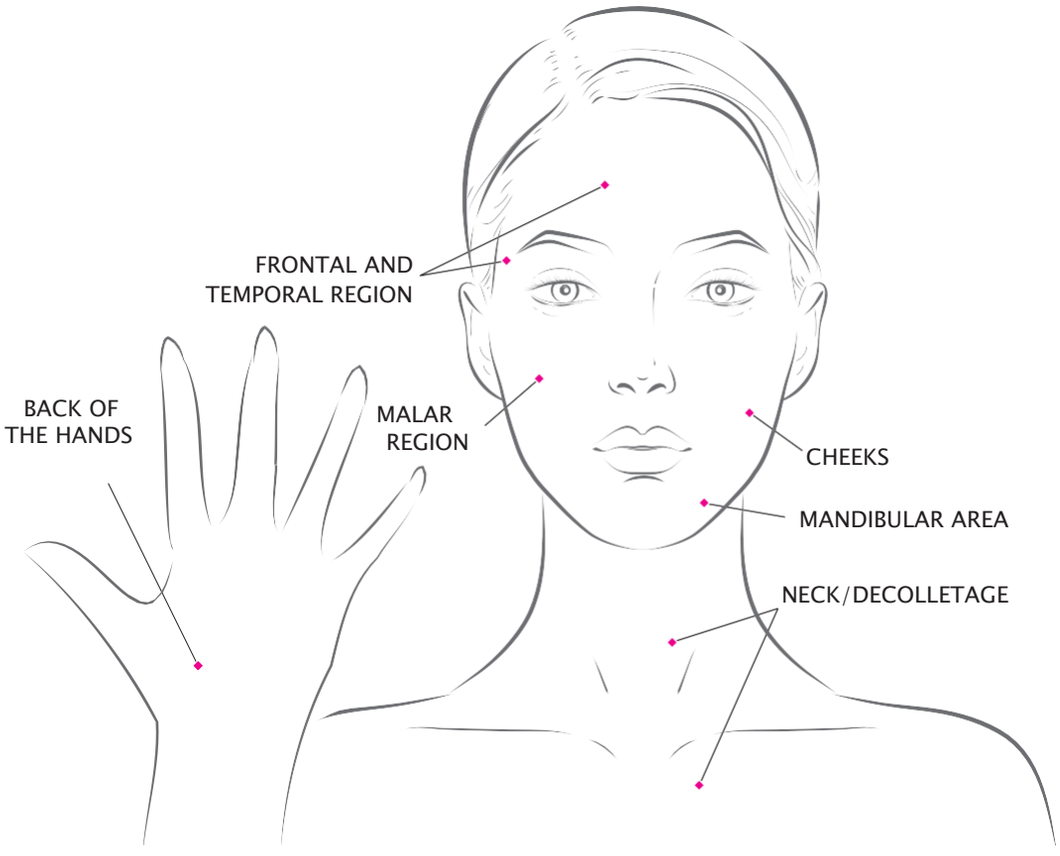
MOLECULAR WEIGHT 2 M Da + 1 M Da Cross-linked HA + 10% Linear HA 500,000 Da

CROSS-LINKING AGENT BDDE residue < 0.1 ppm

MODULUS OF ELASTICITY G' 30 Pa

MODULUS OF VISCOSITY G" 10 Pa

PLANE OF INJECTION Middle dermis



4. INDICATIONS ACCORDING TO AREA OF TREATMENT

The Guide aims to support the practitioner by providing information about the specifications of the product and how to obtain the best possible results when using it. Based on his or her experience, the practitioner will select which protocols and techniques to use on a case-by-case basis, and may even decide to combine them if they see fit.

4.1. FACE - LIFTING BIO-RESTRUCTURING

INJECTION TECHNIQUES:	Linear with needle 30 G x 13 mm Deep (non-superficial) intradermal micro-ponfi with 30 G x 4 mm needle Linear with 25 or 27 G cannula
MODES OF USE:	Working upwards from the base for lifting effect.

Protocol by
Dr Enrico Massidda
Cosmetic Physician

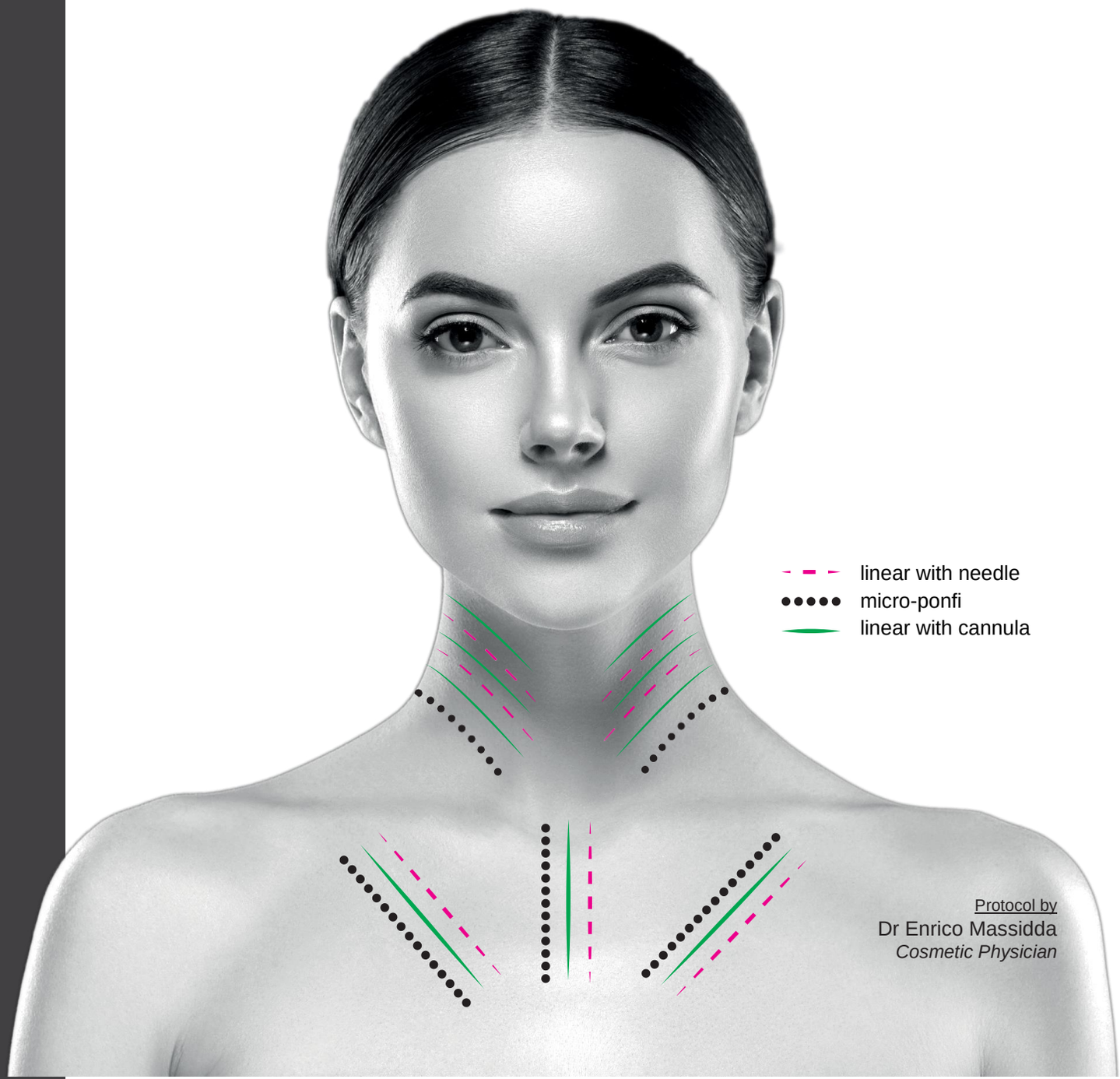
4.2. NECK

INJECTION TECHNIQUES: Linear with needle 30 G x 13 mm
Deep (non-superficial) intradermal micro-ponfi with 30 G x 4 mm needle
Linear with 25 or 27 G cannula

MODES OF USE: Working upwards from the base for lifting effect.

4.3. DÉCOLLETAGE

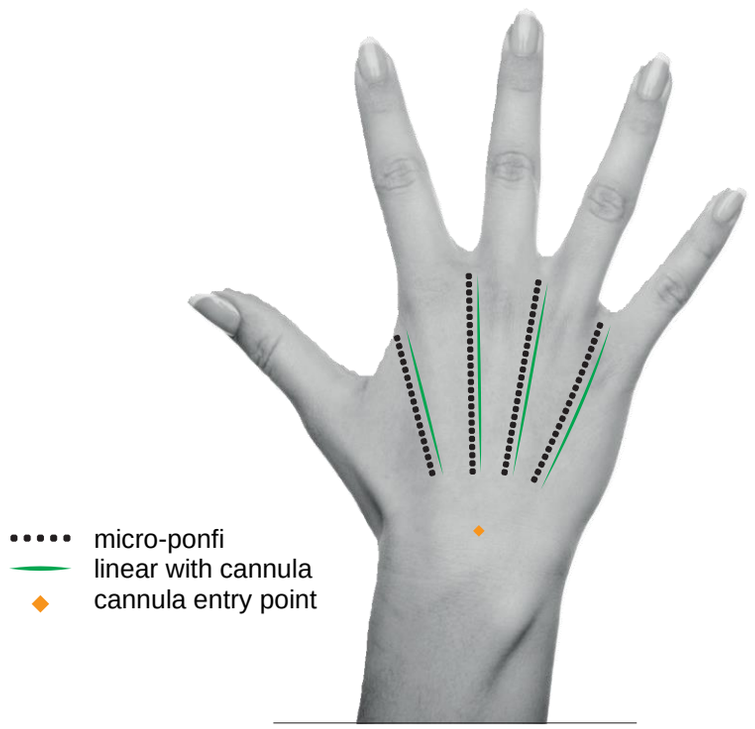
INJECTION TECHNIQUES: Linear microdepot injections with 30 G x 13 mm needle
Deep (non-superficial) intradermal micro-ponfi with 30 G x 4 mm needle
Linear with 25 or 27 G cannula



Protocol by
Dr Enrico Massidda
Cosmetic Physician

4.4. HANDS - BIORESTRUCTURING

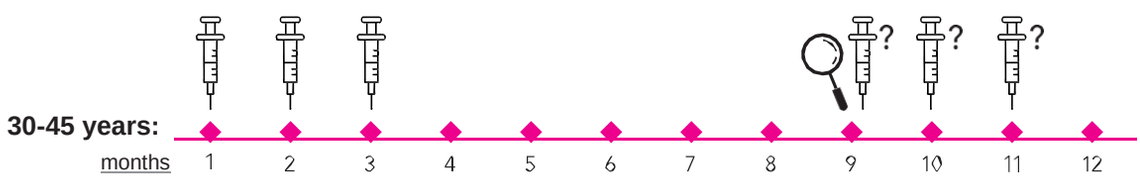
INJECTION TECHNIQUES: Linear with 25 or 27 G cannula
Deep (non-superficial) intradermal micro-ponfi with 30 G x 4 mm needle



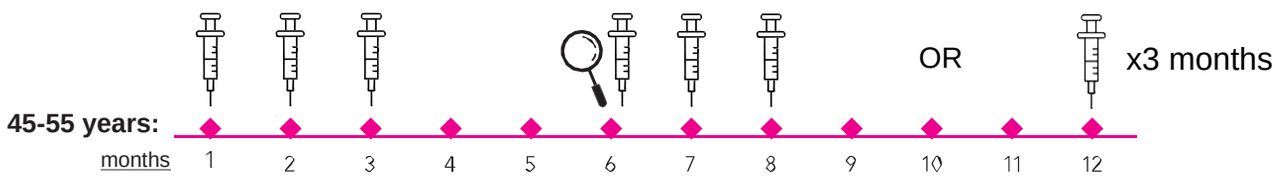
Protocol by
Dr Enrico Massidda
Cosmetic Physician

5. PROTOCOLS

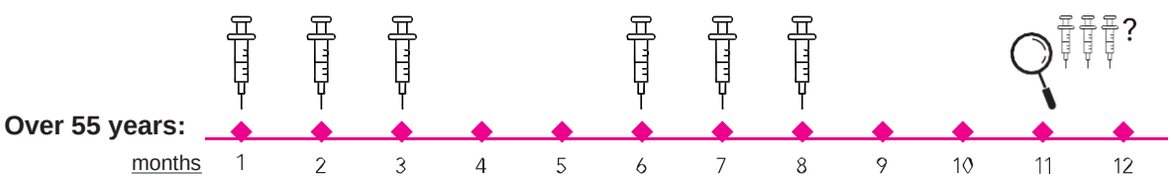
(Valid for each area of treatment)



1 session per month x 3 months, follow up at 6 months; repeat cycle if necessary.



1 session per month x 3 months, follow-up at 3 months;
repeat the cycle if necessary, and after 6 months.



1 session per month x 3 months, follow-up at 3 months;
repeat the sessions; follow-up at 3 months; repeat the cycle if necessary.

6.

AGEX*fill* VOLUME

Indicated for correcting medium facial volumes, it adapts to the patient's morphology while respecting the natural facial features.

CHARACTERISTICS
- Volume
- Restructuring
- Filling

SUPPLIED WITH
- 27 G x 13 mm needle
- 27 G x 19 mm needle

COMPATIBLE WITH
- 25 G x 38 mm / 50 mm cannula

TECHNICAL DATA SHEET

PACKAGE CONTAINS 1 pre-filled disposable syringe

DOSAGE 1 ml

COMPOSITION Cross-linked and linear hyaluronic acid (with Hyalobilayer® technology)

CONCENTRATION 25 mg/ml

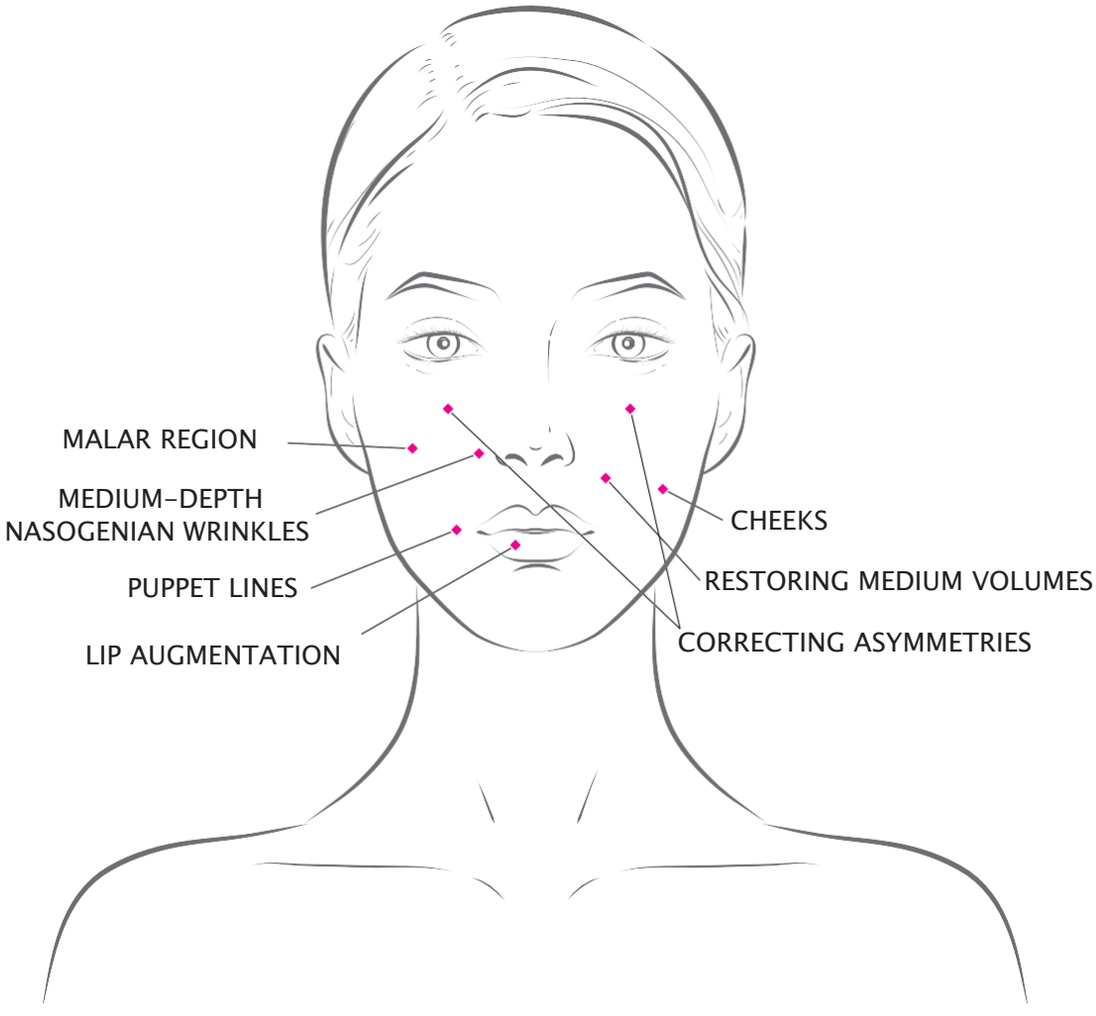
MOLECULAR WEIGHT 1M Da + 2M Da Cross-linked HA + 8% Linear HA 1M Da

CROSS-LINKING AGENT BDDE residue < 0.1 ppm

MODULUS OF ELASTICITY G' 100 Pa

MODULUS OF VISCOSITY G' 20 Pa

INJECTION PLANE Hypodermis



6.1. CLINICAL STUDY

REAL-WORLD OUTCOMES OF LIP AUGMENTATION USING A HYALURONIC ACID-BASED FILLER WITH LOW BDDE CONTENT: A PROSPECTIVE, OPEN-LABEL, MULTICENTRE, POST-MARKETING STUDY

FULL https://bit.ly/3HKWnJt

Enrico Massidda, et al. - Cureus

Introduction

1,4-Butanediol diglycidyl ether (BDDE) is the most common cross-linker used to produce hyaluronic acid (HA)-based dermal fillers. However, BDDE may have cytotoxic and potentially mutagenic effects, raising safety concerns. Consequently, manufacturers are developing new HA filler formulations with reduced BDDE levels to mitigate potential biological risks.

Aim

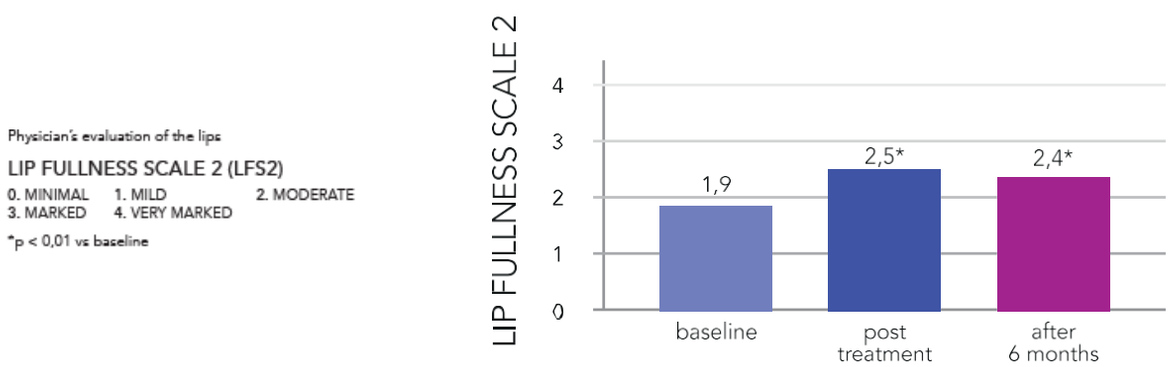
To evaluate the clinical outcomes of lip augmentation performed using a HA-based filler with reduced BDDE content (Agex FillVolume®) in a real-world clinical setting.

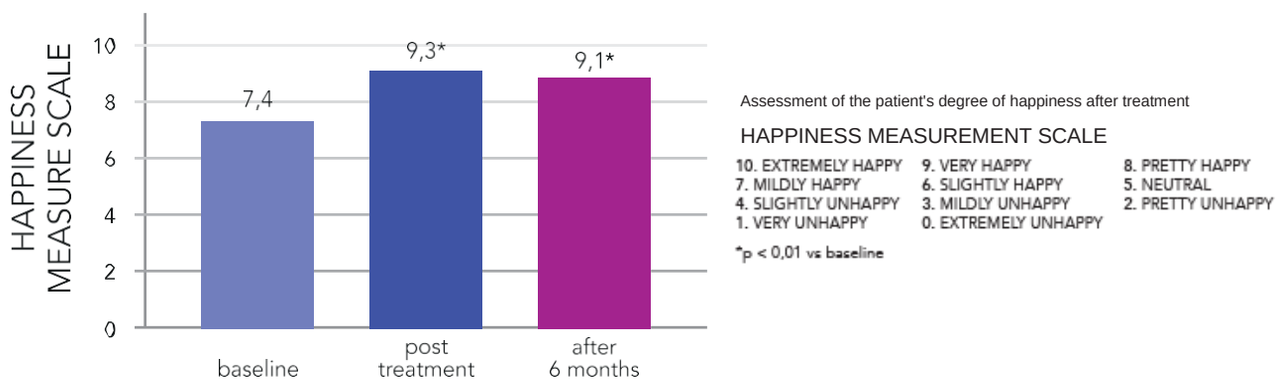
Results

73% of the study participants (22/30) demonstrated an improvement of at least one point in their LFS2 scores post-treatment, compared to baseline, thus qualifying as responders. Six months later, the responder rate, based on LFS2 scores, remained steady at 66.7% (20/30). Importantly, these aesthetic improvements were consistently associated with a positive impact on subject-reported HMS, with a significant difference ($p < 0.001$) between post-treatment and baseline scores. All adverse events reported after treatment were mild.

Conclusions

Agex FillVolume®, a HA filler with low BDDE content, provides a safe and effective option for enhancing lip volume in real-world aesthetic settings.





7. AGEX*fill* ULTRA

Ideal for revitalising deep facial volumes and correcting major skin sagging.

CHARACTERISTICS
- Deep volumes
- Deep skin sagging

SUPPLIED WITH
- 25 G x 38 mm cannula
- 23 G x 19 mm needle

COMPATIBLE WITH
- 27 G x 13 mm needle

TECHNICAL DATA SHEET

PACKAGE CONTAINS 1 pre-filled disposable syringe

DOSAGE 1 ml

COMPOSITION Cross-linked and linear hyaluronic acid (with Hyalobilayer® technology)

CONCENTRATION 25 mg/ml

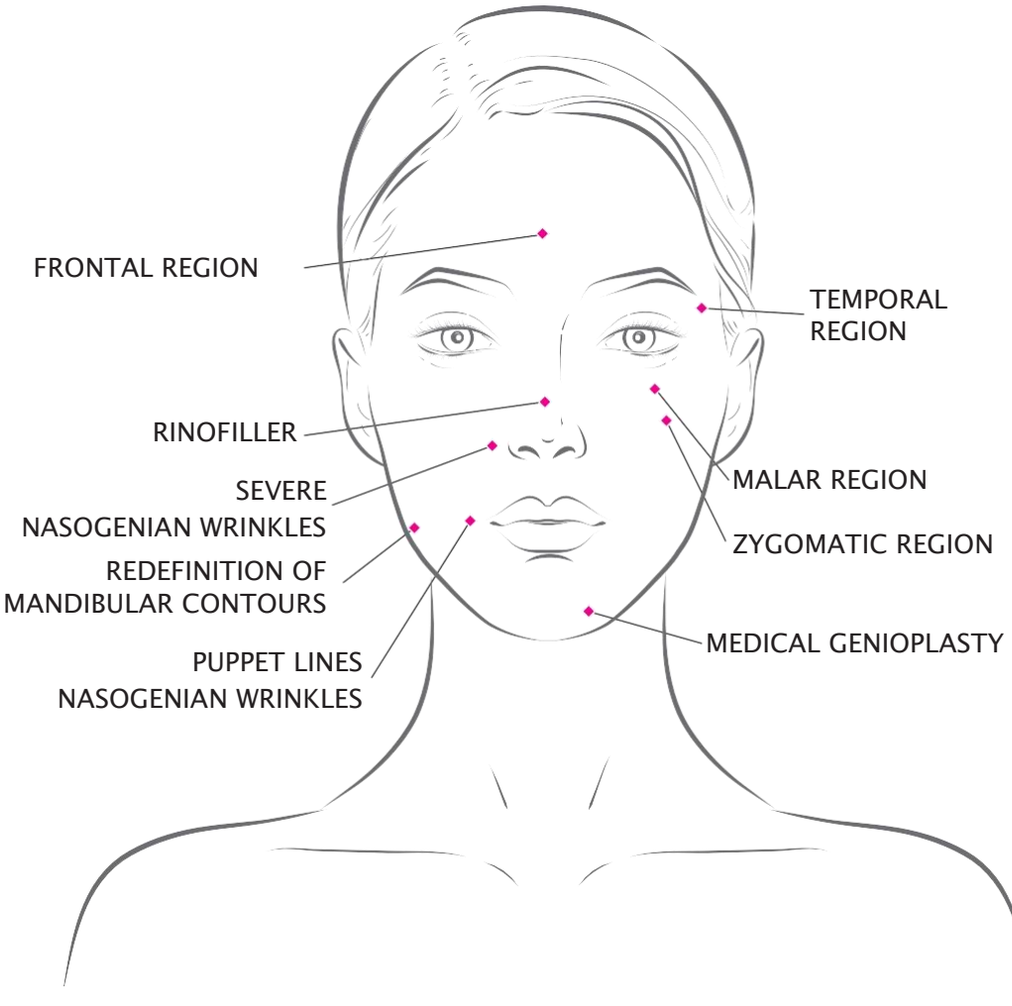
MOLECULAR WEIGHT 1 M Da + 2 M Da cross-linked + 5% linear HA 500,000 Da

CROSS-LINKING AGENT BDDE residue < 0.1 ppm

MODULUS OF ELASTICITY G' 200 Pa

MODULUS OF VISCOSITY G" 40 Pa

PLANE OF INJECTION Deep hypodermis, periosteum



7.1. IN VITRO STUDY

FULL VERSION

https://pubmed.ncbi.nlm.nih.gov/36686003/

HUMAN DERMAL FIBROBLAST RESPONSE TO HYALURONIC ACID-BASED INJECTABLE DERMAL FILLERS: AN IN VITRO STUDY

Simona Varì, et al. - Advances in Dermatology and Allergology

Introduction

Hyaluronic acid (HA)-based injectable dermal fillers (IDFs) used in aesthetic procedures may increase fibroblast activity and ultimately improve subcutaneous tissue quality.

Aim

To further our understanding of fibroblast response to different commercial HA-based IDFs.

Results

All tested IDFs elicited a higher release of type I collagen in NHDF culture supernatants, although Juvederm Voluma was found to induce the most pronounced increase. Agex Fill Ultra induced the highest production of type III collagen and elastin. Levels of TGF-β1 and type I collagen in cell culture supernatants were positively correlated to each other ($r = 0.57$, $p < 0.05$). Conversely, 8-OHdG concentrations were inversely associated with both type III collagen ($r = -0.41$, $p < 0.05$) and elastin ($r = -0.46$, $p < 0.05$).

Conclusions

Juvederm Voluma resulted in a high formation of type I collagen

AGEXFILL ULTRA stimulated the production of type III collagen and elastin

Teosyal Ultra Deep and Belotero Intense did not stand out in the stimulation of collagen and elastin

Of the fillers tested, **AGEXFILL ULTRA** proved to be the best in terms of safety, having the least oxidising and genotoxic potential, measured using the biomarker 8-OHdG (oxidative DNA damage)

Type I collagen is more plumping, but also denser, more fibrous and less elastic than type III collagen. Type III collagen is typical of young skin

With age, type III collagen tends to decrease in the skin while type I increases

Oxidative DNA damage may contribute to an increased deposition of type I collagen, ultimately resulting in fibrotic sequelae

AGEXFILL ULTRA stimulates an 'elastic' oriented phenotype, whereas Juvederm Voluma stimulates a 'fibrous' phenotype (as also shown by the increase in TGF-β1)

Our findings suggest that a low BDDE may favour the expression of type III collagen and elastin

Table 1. Hyaluronic acid-based injectable dermal fillers tested in the study

Filler name	Company	HA concentration [mg/ml]	Cross-linker	Properties
Agex Fill Ultra	Biodue SpA	25	BDDE	Consists of Crosslinked and linear (5%) hyaluronic acid; low BDDE content (< 0.01 ppm)
Juvederm Voluma	Allergan	20	BDDE	Consists of Crosslinked hyaluronic acid (produced by Streptococcus equi) in physiologic buffer
Teosyal Ultra Deep	Teoxane SA	25	BDDE	Characterized by a high amount of Crosslinked HA with a high elastic modulus and high cohesivity
Belotero Intense	Merz	25.5	BDDE	Characterized by a high amount of Crosslinked HA; cohesive (monophasic) polydensified filler

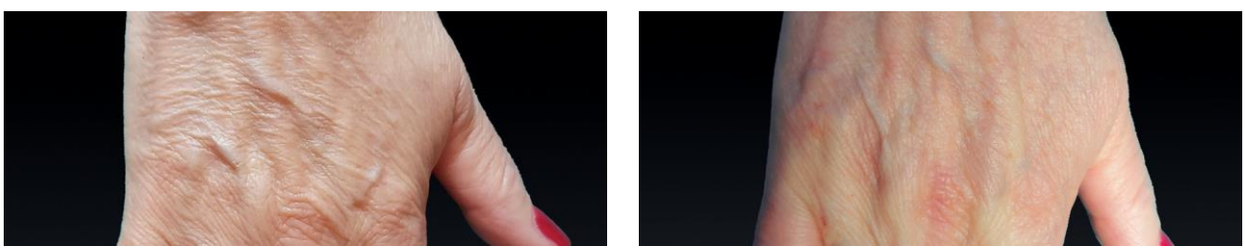
8. BEFORE/AFTER TREATMENT

NECK | 1 x 1.1 ml Agex Fill per side

LIPS | 1 x 1,1 ml Agex Fill

CHEEKS | 1 x 1.1 ml Agex Fill each side

HANDS | 1 x 1.1 ml Agex Fill



FULL FACE | 3 x 1.1 ml Agex Fill (1x3 sessions - result after 3 months)

9. PRE-TREATMENT INDICATIONS

9.1. FOR THE PATIENT

PRE

- Inform your doctor of any allergies or illnesses
- Do not take substances that could thin the blood (e.g. aspirin, NSAIDs, alcohol) in the 48 hours preceding treatment.

9.2. POST-TREATMENT

POST

- Avoid strenuous exercise for 24-48 hours
- Do not take substances that could thin the blood (e.g. aspirin, NSAIDs, alcohol) for 48 hours following treatment
- Do not use make-up for at least 12 hours
- Avoid saunas, steam baths and exposure to sunlight and UV lamps on the days following treatment.
- If the treated area swells, apply an ice pack.

AGEX is a brand of
Biodue S.p.A. - Via Lorenzetti 3/A – 50028
Loc. Sambuca V.P. - Barberino Tavarnelle (FI) - ITALY
info@agexbeauty.com

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by PHARCOS

FEEL NATURAL BEAUTY

www.agexbeauty.com