

PROFHILO®



Alma
For You. For Life.

EVERYONE IS A MASTERPIECE.



Caring Innovation



“

*“I firmly believe that **the primary role of our company is to focus on the needs of patients and healthcare professionals**, through the work of a well-trained, and above all, satisfied and motivated group.”*

”

Arturo Licenziati
President & CEO - IBSA GROUP

IBSA GROUP

Founded by a group of Swiss biologists in 1945, IBSA - Institute Biochemical SA - has gained unique experience in pharmaceutical research and technology. IBSA has used its experience and expertise in the pharmaceutical field to branch out and develop medical devices for dermatology based on hyaluronic acid - thus creating a dedicated dermoaesthetic brand: **IBSA Derma**. IBSA Derma distinguishes itself in this vast market because it controls the entire product lifecycle, from the biofermentation production of the raw material to the ready-to-use final product in pre-filled syringes.

OVER **25** OFFICES &
MANUFACTURING
PLANTS

HUNDREDS OF
PRODUCTS COVERING
9 THERAPEUTIC AREAS

PRODUCTS AVAILABLE
IN MORE THAN **80**
COUNTRIES

IBSA IS ONE OF THE LEADING
PHARMACEUTICAL COMPANIES
IN **HYALURONIC ACID PRODUCTION**
& **PRODUCTS** CONTAINING HA

SCIENTIFIC KNOWLEDGE

TECHNOLOGICAL DEVELOPMENTS

FULL PRODUCTION PROCESS CONTROL
HA raw material - finished product

STATE OF THE ART PRODUCTION PLANTS



The IBSA Derma approach is aimed at countering the physiological decrease of hyaluronic acid in the skin tissue, thus restoring hydration, elasticity and tone. In fact, in a synergistic way, it combines deep hydration with mechanical action of lifting the skin.

Thanks to its innovative use of ultrapure hyaluronic acid, we can now say that **IBSA Derma has redefined the canons of classical beauty.**

In fact, throughout history, beauty has had well-defined and specific standards. Today this is no longer the case, because **IBSA Derma has redefined the beauty rules while enhancing the authenticity of each individual.**

EVERYONE IS A MASTERPIECE

**IBSA Derma brings out the authentic beauty
in everyone, proving that we are all masterpieces.**

No more faces that look the same and procedures
that may distort the somatic traits, now real people
are the only reference of beauty that counts.

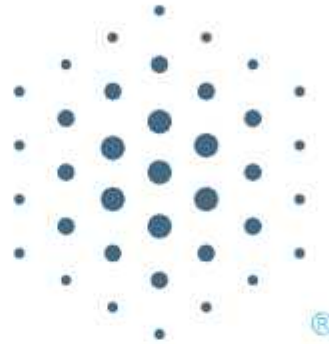
IBSA DERMA PILLARS

IBSA Derma offers a full range of products and brands such as Viscoderm®, Prophilo® and Aliaxin® based on the Hydrolift® Action concept.

Hydrolift® Action is an innovative approach aimed at counteracting the physiological reduction of hyaluronic acid in the skin, restoring hydration, elasticity and skin tone.

Hydrolift® Action is an expression of the synergistic action derived from the use of selected hyaluronic acid produced using patented IBSA technology, which when used in combination, creates optimal conditions for preventing and fighting the aging process.





SHYALT[®]
ULTRAPURE
SODIUM HYALURONATE ALTERGON

IBSA's hyaluronic acid is an ultrapure grade HA, produced through a patented biofermentation process, of *Streptococcus Zooepidemicus*, which ranks worldwide as "TOP HIGH QUALITY" in terms of purity and safety.



PROFHILO®

PROFHILO[®]

for

BIOREMODELING

ITALIAN LAUNCH
February 2015

INTERNATIONAL LAUNCH
January 2016

Over
500.000
treatments performed.
December 2018

BEST PRODUCT AWARDS

2016-2018



Available in

56 COUNTRIES

December 2018



WHAT'S NEW

PROFHILO® stabilized hybrid cooperative complexes is the first product developed with Nahyco®. A unique and innovative thermal production process patented by IBSA.

HOW IT WORKS

PROFHILO® promotes:

MULTI-LEVEL

DYNAMIC

REMODELING

Leading to a remodeling of the extracellular matrix in terms of elasticity and support, promoting and maintaining the viability of:

FIBROBLASTS¹ KERATINOCYTES¹ ADIPOCYTES²

INTENDED USE

TISSUE REMODELING AND IMPROVEMENT IN SKIN LAXITY (face, neck and body).

HOW TO USE

2 sessions with a one-month interval. All aesthetic injection techniques are indicated in the superficial subcutaneous layer.

IBSA recommends the BAP (Bio Aesthetic Points) Techniques in order to minimize the risks and maximize the product's flowability.

PROFHILO[®]

WHAT'S NEW

BEGINNING WITH A SIMPLE MIX:

32 mg of hyaluronic acid

high molecular weight
(1100-1400 kDa)

+

32 mg of hyaluronic acid

low molecular weight
(80-100 kDa)

THERMAL STABILIZATION PROCESS

The simple mix is heated
and cooled according to
IBSA's patented **thermal
production process**
(no chemical cross-linking
agents used)

Production process ●

1

2

HI
+
LS



 **NAHYCO[®]**
HYBRID TECHNOLOGY

Obtaining:
PROFILO®
stabilized hybrid
cooperative complexes

A new tool with

UNIQUE CHARACTERISTICS

HIGH HA CONCENTRATION (64mg/2ml)³

Highly manageable⁴

Extensive spreadability⁵

Low viscosity⁴

No BDDE or other chemical agents³

Low inflammatory response⁴

Thermally stabilized **natural HA**
with a duration comparable to
a low cross-linked gel⁵

→ **PROFILO®**



PROFHILO®

HOW IT WORKS "IN VITRO"



MULTI-LEVEL

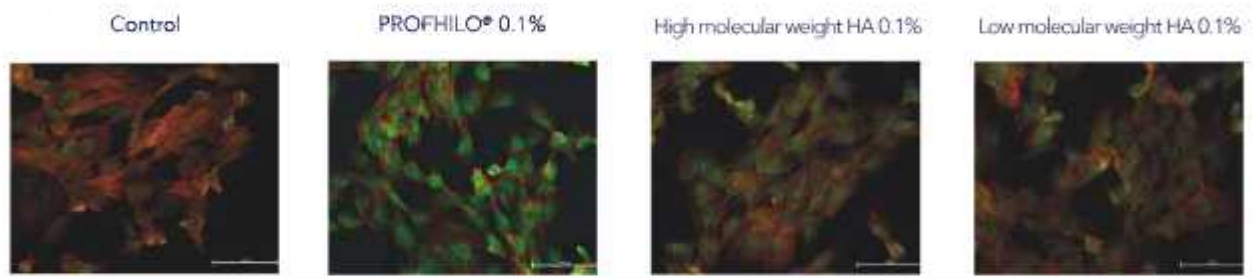
DYNAMIC

REMODELING

In vitro studies have shown that PROFHILO® improves the extracellular environment:¹⁻²

- Maintaining suitable conditions for the viability of fibroblasts, keratinocytes and adipocytes.
- Leading to a remodeling of the extracellular matrix in terms of elasticity and support.

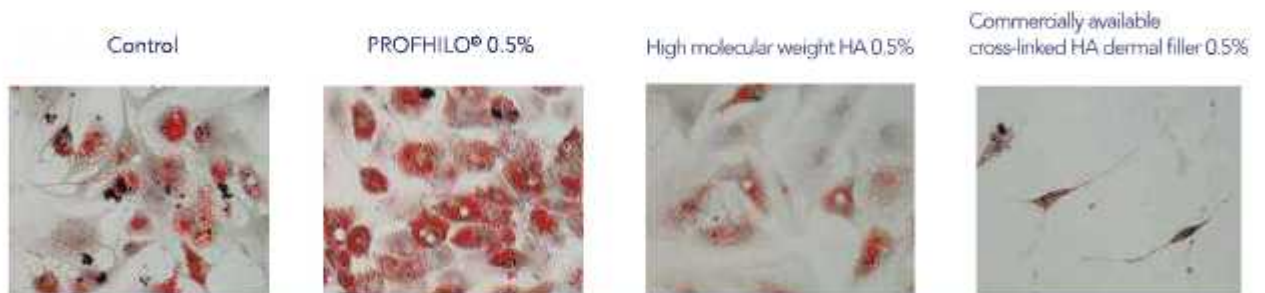
KERATINOCYTES-FIBROBLASTS: PROFHILO® INCREASES ELASTIN EXPRESSION.



In vitro keratinocytes-fibroblasts immunofluorescence pictures relative to elastin expression¹

● Elastin

ADIPOCYTES: PROFHILO® SUPPORTS VIABILITY.



In vitro Oil Red O staining performed on Adipocyte Stem Cells in adipogenic medium, 14 days after incubation²

● Fat deposits Courtesy of Bioteknet

PROFHILO® IN THE TISSUE

An important characteristic due to the high cohesivity of PROFHILO® is its optimal tissue integration capacity.⁵

PROFHILO®'s behavior in the skin reflects a unique biophysical profile; particularly, a predominance of fluidity over elasticity ($\tan \delta > 1$) which is not present in cross-linked gels.⁵

Notable for its ability to flow uniformly through entire anatomic units after injection and therefore homogeneously expanding fat compartments in challenging areas where even low viscosity fillers can produce contour irregularities.⁵

The IBSA GPS Scale is based on actual rheological data:

GPS GUIDE TO
PRODUCT
SELECTION
SCALE



COHESIVITY



FLOW



LIFT



SCULPT

Adapted with permission
from: Sundaram H, Cassuto D,
Gevard Mollard S (publication in
preparation).

PROFHILO®

INTENDED USE

TISSUE REMODELING AND IMPROVEMENT IN SKIN LAXITY

FACE



NECK



BODY



PROFHILO® intervenes:

in the physiological process of aging tissue, in presence of alterations in elastic fibers and collagen.

In the dermal tissue repair process, in cases of acne or scars.

In case of loss or compromised adipose tissue.



PROFHILO®

HOW TO USE

THE

BAP TECHNIQUES

(BIO AESTHETIC POINTS)

Originally created for the malar and sub-malar areas due to their predisposition to dermal atrophy caused by the aging phenomena, the BAP Technique is the most widespread and highly recommended protocol for treating these areas⁶⁻⁹.

Owing to PROFHILO®'s high flowability, without leaving tissue irregularities, a specific BAP Technique was developed for the neck.

Thanks to the unique rheological characteristics of Profhilo®, TISSUE remodeling is easily obtained in only 2 SESSIONS* (1 MONTH INTERVAL) using all Aesthetic injection techniques, in the superficial subcutaneous layer.

* Number of treatments and product quantity depend on the degree of aging.

REMODELING THE MALAR & SUBMALAR AREAS

These 5 points identify the 5 anatomically receptive areas of the face with an absence of large vessels and nerve branches, therefore, minimizing the risks while maximizing the diffusion of the product in the malar and submalar areas.

Identify the 5 BAP
injection sites on each
side of the face

Inject 0.2 ml per
bolus at the superficial
subcutaneous layer

1 ZYGOMATIC PROTRUSION

at least 2 cm away from the external corner of the eye

2 NASAL BASE

- draw a line connecting the nostril and tragus
- draw a perpendicular line starting from the pupil
- locate the injection point at the intersection of the 2 lines

3 TRAGUS

1 cm anterior to the bottom of the tragus

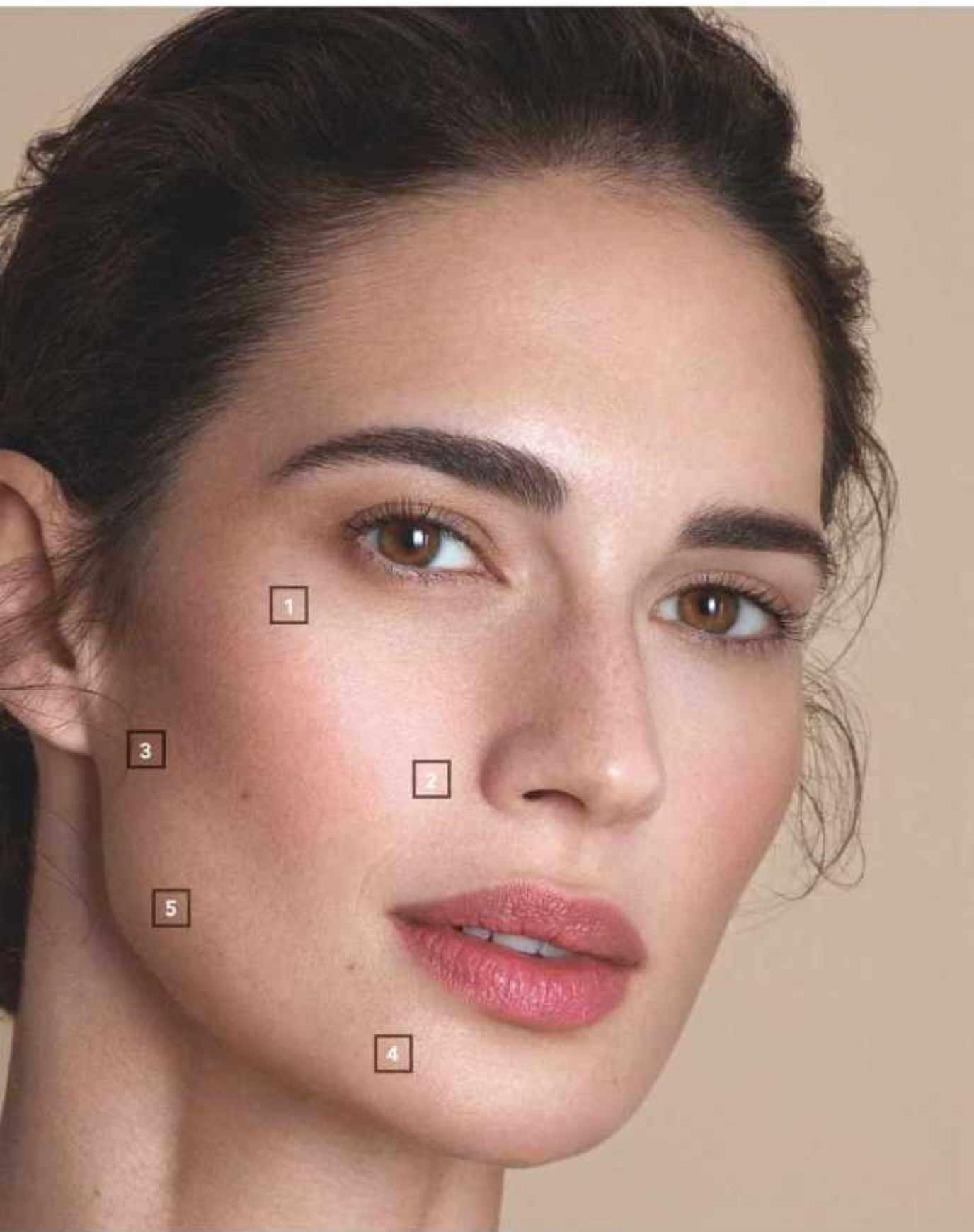
4 CHIN

- draw a vertical line in the center of the chin
- draw a perpendicular line one third from the top of the vertical line
- from the point of intersection move 1.5 cm towards the oral commissures

5 MANDIBULAR ANGLE

1 cm above the mandibular angle





This image is for illustrative purposes only and is intended to convey the concept and vision of the Profhilo® BAP Technique. Do not use this image as a sole reference to perform the treatment.

NECK

REMODELING

The 10 point BAP Neck Technique was developed in order to: provide reproducible points of injection, standardize these points irrespective of variations between patients and ensure that the injection points avoid potential injury to vital structures.

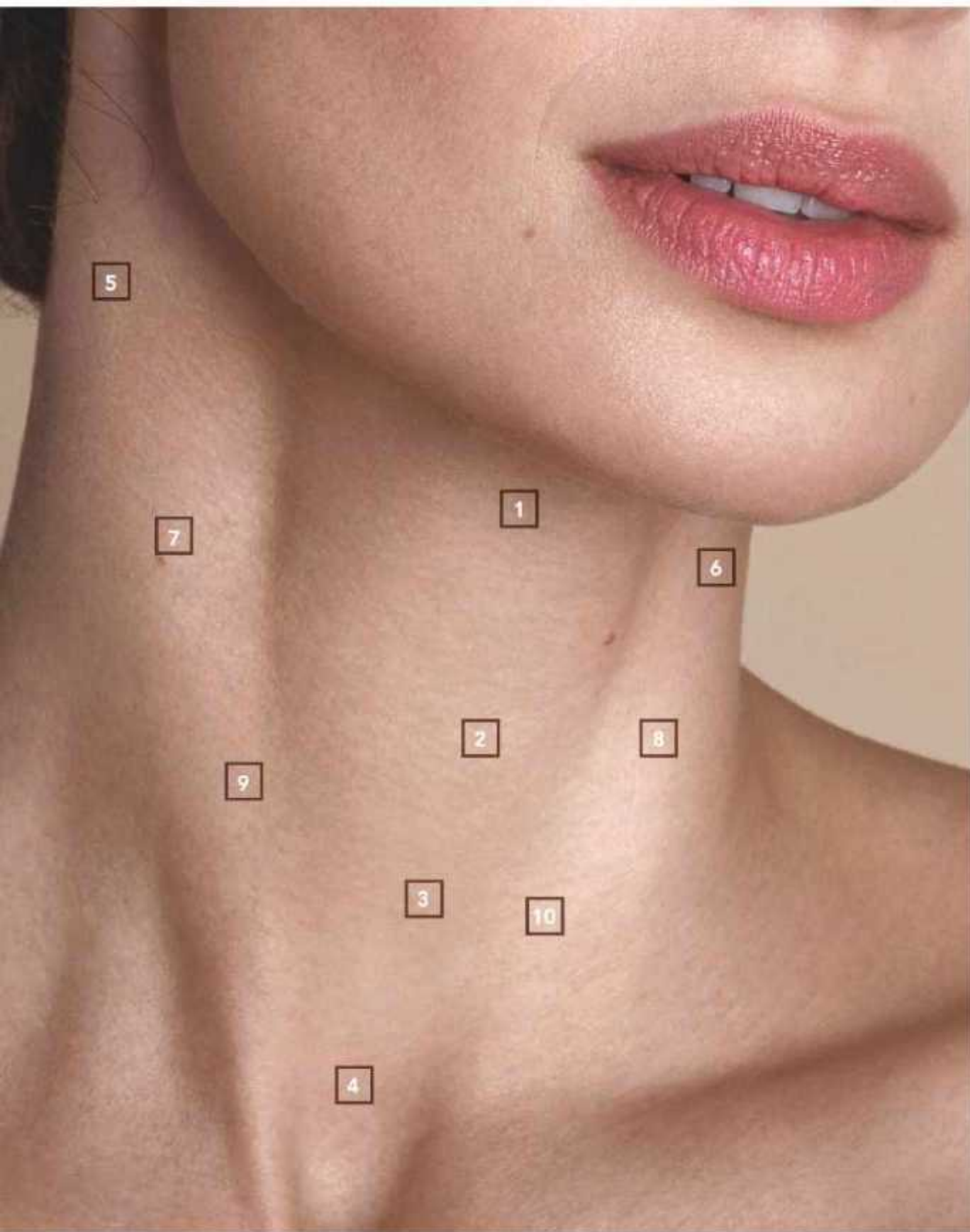
Identify the 10 BAP injection sites on the neck

Pinch the skin at the injection point

Inject 0.2 ml per bolus transversely across the skin at the superficial subcutaneous layer

- 1 Midline between the submental border and hyoid bone
- 2 Midline between the apex of Adam's Apple and bottom of thyroid cartilage
- 3 Midline between the base of thyroid cartilage and sternal notch
- 4 Midline at the apex of sternal notch
- 5 Horizontal line with mandibular angle & 0.5 cm lateral
- 6 to medial border of the SCM (sternocleidomastoid muscle)
- 7 Horizontal line between apex of Adam's Apple and
- 8 bottom of thyroid cartilage
- 9 Horizontal line between the base of thyroid cartilage
- 10 and sternal notch



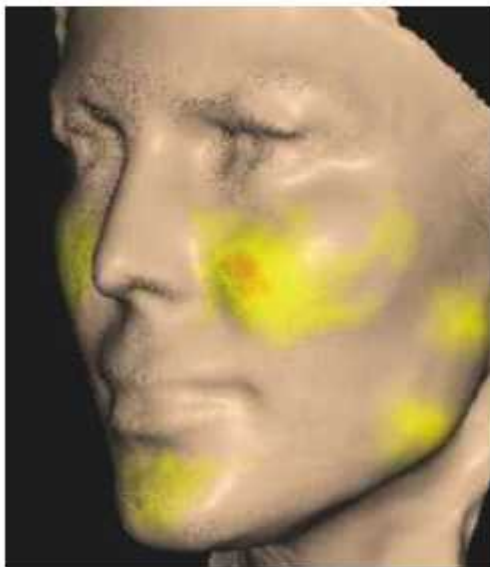


This image is for illustrative purposes only and is intended to convey the concept and vision of the Profhilo® BAP Neck Technique. Do not use this image as a sole reference to perform the treatment.

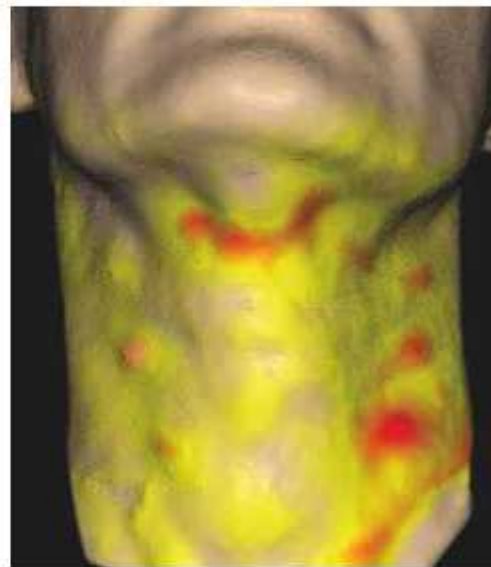
PROFHILO®

HOW IT WORKS "IN VIVO"

PROFHILO® FLOWABILITY EVIDENCE BASED PERSPECTIVE



3D images taken 15 minutes after
PROFHILO® BAP Face and Neck Treatments



Images taken with 3D LIFEVIEW
mini camera from Quantificare

- Visualization of volume changes using a color code in the QuantifiCare software suite.
- Yellow indicates a positive change in volume from the 3D photo taken before treatment, confirming Profhilo®'s spreadability.
- Red indicates greater volume change in the points injected towards the end of the treatment.



Courtesy of Dr. Hema Sundaram (USA)
and Dr. Antonello Tateo (Italy)

PRODUCT QUANTITY/NEEDLE	2 ml - 29G x 13mm
TREATMENT SESSION	2 treatments (1 month interval)
FREQUENCY	twice per year



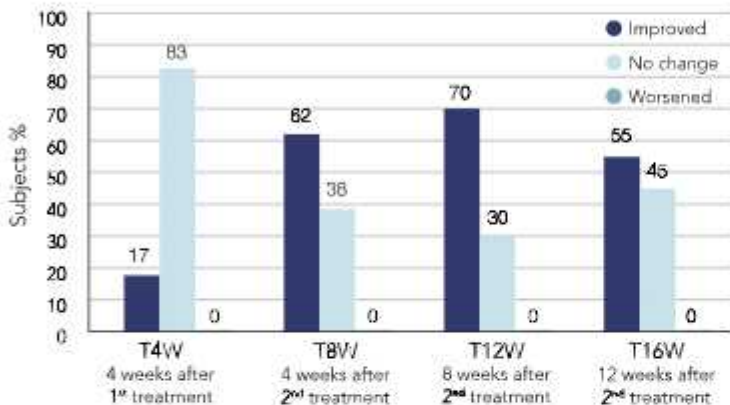
Courtesy of Dr. Emma Ravichandran
(Glasgow, Scotland)

PRODUCT QUANTITY/NEEDLE	1 ml per side - 29G x 13mm
TREATMENT SESSION	2 treatments (1 month interval)
FREQUENCY	twice per year

PROFHILO[®]

RESULTS

PROFHILO[®]'s tightening action has a positive effect on facial volume⁶



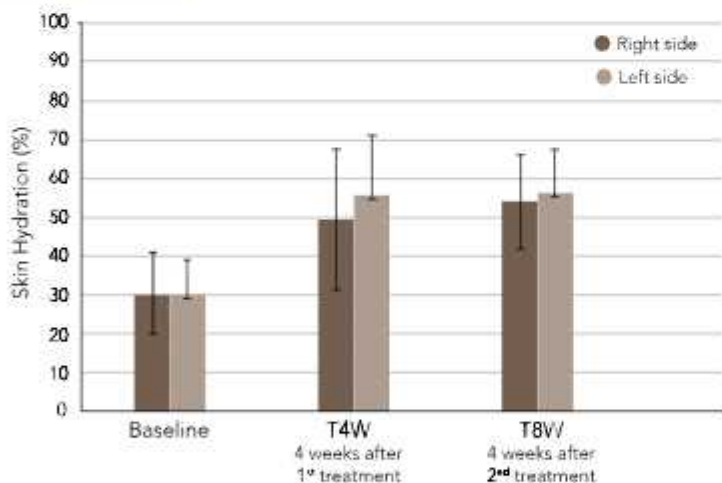
Evaluation on 64 female patients treated using BAP technique

Average age 53 yrs
(Range 38-60 yrs)

FVLS
(Facial Volume Loss Scale range 2-3)

70% of subjects show an improvement of at least one grade according to the FVLS

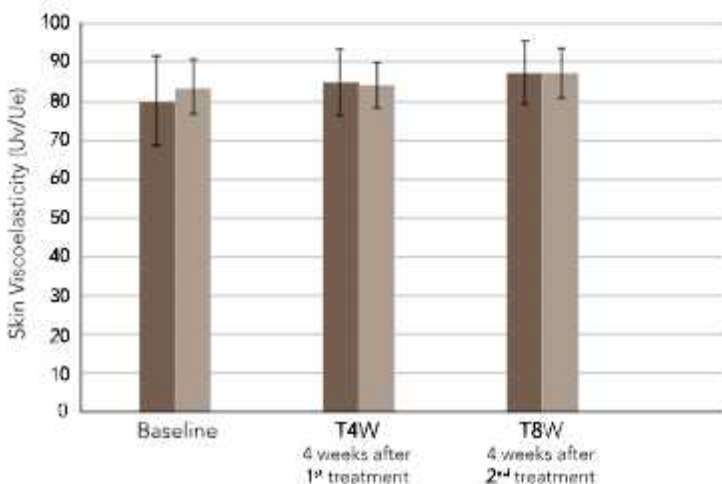
Improved hydration and elasticity⁹



Evaluation on 15 female patients treated using BAP technique

Average age 53 yrs
(Range 39-65 yrs)

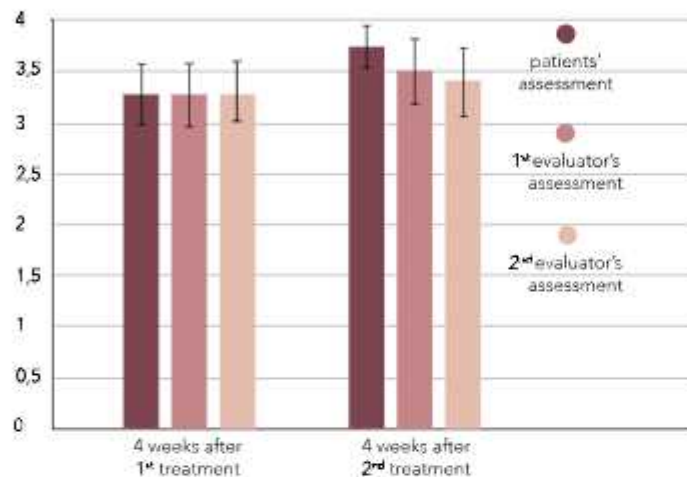
*p value <0.05



Significant improvement in skin hydration after only one treatment and in skin elasticity after two treatments

CLINICAL EVALUATIONS

High satisfaction of doctors and patients⁸



Evaluation on 30 female patients treated using BAP technique

Average age 53 yrs
(Range 40-68 yrs)

Significant improvement of satisfaction levels after the second treatment

Profhilo[®] shows a significant improvement of the skin parameters and a noticeable aesthetic outcome⁵.

Based on these characterizations, Profhilo[®] represents an intriguing new paradigm for skin restoration and improvement of skin laxity⁵.

Profhilo[®] has significant potential for synergistic combination with conventionally cross-linked fillers to finesse volumetry results⁵.

PROFHILO®

IN VITRO AND CLINICAL STUDIES

In vitro analysis of the effects on wound healing of high and low molecular weight chains of hyaluronan and their hybrid H-HA/L-HA complexes.

D'Agostino A. et al.

BMC Cell Biol 2015;16:19.

SUMMARY

[...] In this study, low molecular weight HA (L-HA) proved not to be toxic/inflammatory, and therefore permitted wound closure similarly to the well-known bioactive high molecular weight HA (H-HA). Novel hybrid complexes formed by H-HA and L-HA performed better than HA alone, both at high or low concentrations. Complexes also showed better stability of long chains HA to hyaluronidases attack, presumably prolonging their half-lives in vivo. L-HA accelerates wound repair at an earlier stage, while H-HA has no short-term effect, probably due to its initial higher viscosity. The outcomes of this study may be the pillars for further in vivo studies to promote HA hybrid complex use in innovative medical devices for tissue regeneration. [...]

Full text available on PubMed, PMID: 26163378



Hyaluronan hybrid cooperative complexes as a novel frontier for cellular bioprocesses reactivation.

Stellavato A. et al.

PLoS One 2016;11(10):e0163510.

SUMMARY

[...] In this study, the multi-faceted interaction between keratinocytes and dermal fibroblasts in presence of the novel hybrid cooperative complexes HA formulation was evaluated. The in vitro model employed, has made possible the functional interaction between the two cell types, involving the synthesis and assembly of the skin ECM proteins. The results showed a notably different biological response, regarding collagen and elastin expression and synthesis, of HA hybrid cooperative complexes respect to native HA formulations. A key feature of the hybrid cooperative complexes was the prolonged stability to enzymatic attack, despite the absence of chemical cross linking. These findings could overall corroborate the in vivo clinical data obtained on the HA hybrid cooperative complex38. [...]

Full text available on PubMed, PMID: 27721763



Hybrid Complexes of High and Low Molecular Weight Hyaluronans Highly Enhance HASCs Differentiation: Implication for Facial Bioremodeling.

Stellavato A. et al.

Cell Physiol Biochem 2017;44:1078-1092.

SUMMARY

[...] In this study we demonstrate for the first time that HCCs potentiate ASCs differentiation, preserving both morphology and viability. The quality and the efficiency of the differentiation are greater than that obtained with the other HA formulations, both in terms of gene, protein and morphological expression, and with the formation of large and numerous lipid vacuoles. This is of major importance in clinical use. We can assume that this substance can affect the differentiation of resident fat cells that are present in both the dermis and hypodermis, and counteract the effect of "resorption" of the fat compartment, that is typical of aging. [...]

Full text available on PubMed, PMID: 29179206



Efficacy, safety, and tolerance of a new injection technique for high and low molecular weight hyaluronic acid hybrid complexes.

Laurino C. et al.

Eplasty 2015;15:e46.

SUMMARY

[...] In the current evaluation, we demonstrated efficacy, safety, and tolerance of a new skin rejuvenation procedure with high- and low-molecular-weight HA hybrid complexes injected into the lower impedance subdermal facial areas. The injection of bio-revitalizing medical devices in lower impedance sites has some advantages. The product can stimulate cell proliferation in the facial adipose tissue, which is a source of noncommittal stem cells that differentiate into cutaneous fibroblasts. The physician judged it easy to inject. Patients were very satisfied at the end of the treatment (87.9%) and the compound's outcome evaluated by the physician was optimal in 51.5% of the cases and good in 45.5%. None of the patients expressed negative opinions, and no pain was reported. [...]

Facial bioremodeling by intradermal injection of a stabilized hybrid complex of high and low molecular weight hyaluronic acid: prospective study on 30 patients.

Rodríguez Abascal M. et al.

Eur Aesth Plast Surg J 2015;5(2):124-131

SUMMARY

[...] Use of the stabilized hybrid high and low molecular weight HA complexes via intradermal injection with the BAP technique to improve facial aging, skin texture, reduce laxity and attenuate fine wrinkles proven to be effective, with a very low rate of complications and no other adverse reactions. Furthermore, it is important to highlight the high level of satisfaction among patients. Similarly, from a safety perspective, it is worth noting the low rate of complications resulting from the study, as well as that all the adverse events that arose were derived from the application technique and not inherent to the product. [...]

Efficacy and tolerance of an injectable medical device containing stable hybrid cooperative complexes of high and low molecular weight hyaluronic acid: a monocentric 16 weeks open-label evaluation.

Sparavigna A. et al.

Clin Cosmet Invest Dermatol 2016;9:297-305

SUMMARY

[...] The results of this explorative prospective study, evaluating the clinical efficacy and tolerability, clearly supports the bio-remodeling and rejuvenation claim of the hybrid cooperative complexes. All subjective clinical outcomes and the majority of objective instrumental results indicate a rapid and statistically significant improvement in the face attractiveness parameters. In particular, the volumetric and tightening effects were significant and maintained until the end of the study. From week 8, filling, anti-wrinkle, plumping, and hydrating activities become statistically significant, as measured by the reduction of WSR score, profilometric, torsionometric, and skin electrical capacitance parameters. These instrumental and clinical findings are also confirmed by the photographic documentation. [...]

Hyaluronic acid hybrid cooperative complexes and the BAP (Bio Aesthetic Points) technique: the new edge in biorejuvenation.

Boatini A. et al.

Aesthetic Medicine 2016;2(2)

SUMMARY

[...] Objectivity in the post-treatment showed better skin turgor (similar to a tightening effect), brighter skin, reduced nasolabial fold depth and improved texture and pigmentation. The patients reported having experienced less pain and less bruising than traditional biostimulation. They appreciated the reduced time and number of sessions, and were generally satisfied with the overall improvement of the face and long lasting results. The hybrid cooperative complexes treatment of skin laxity, wrinkles and folds of the middle and lower third of the face resulted in a significant improvement of skin hydration and viscoelasticity, combined with a high level of compliance and satisfaction referred by the patients. [...]

Full text available on PubMed, PMID: 26491508



Full text available on PubMed, PMID: 27713647



*Summaries were extracted from the studies.

PROFHILO
HAENKENIUM®



PROFHILO HAENKENIUM®

Multi-action antioxidant cream for maintaining cellular vitality.

Face, neck and décolletage remodeling.

Enhances firmness and elasticity and reduces micro-wrinkles.



CONTENTS OF THE PACK

- 1 Airless bottle
- 50 ml of antioxidant cream

PROFHILO HAENKENIUM®

COMPOSITION

Contains a hyaluronic acid (sodium salt) complex with a dual molecular weight and a specific and patented **dry extract of Salvia haenkei:**

HAENKENIUM®.

A patented vegetable extract and a potent antioxidant which has two active properties:

It slows the degradation of hyaluronic acid caused by free radicals, therefore prolonging the benefits to the skin.

It acts as a screen for free radicals, a cause of oxidative stress and premature cell senescence, as proven in scientific studies .

HOW THE FORMULA WORKS

The combination of the hyaluronic acid's two different molecular weights causes a synergistic effect which benefits the skin; the high-molecular-weight hyaluronic acid protects by maintaining the integrity of the hydrolipidic film, meanwhile, the low-molecular-weight hyaluronic acid keeps the skin perfectly hydrated thanks to its special hydrophilic properties. The Salvia haenkei extract acts as gerosuppressant, decreasing cellular senescence by 50%.

RESULTS

The synergistic effect of combining two molecular weights of hyaluronic acid helps to restore firmness and elasticity as well as soothe sensitive, irritated and reddened skin.



Salvia haenkei

PROFHILO HAENKENIUM®

Thanks to its combination of hyaluronic acid and HAENKENIUM®, also diminishes visible signs of aging such as wrinkles while restoring skin firmness and elasticity.

CLINICAL STUDIES CONFIRM:

**AN INCREASE OF MORE THAN 40%
OF NATURAL CELLULAR ANTIOXIDANT ACTIVITY
AFTER ONLY TWO WEEKS, AND A REDUCTION
OF THE SIGNS OF PHOTOAGING CAUSED
BY OXIDATIVE STRESS.**

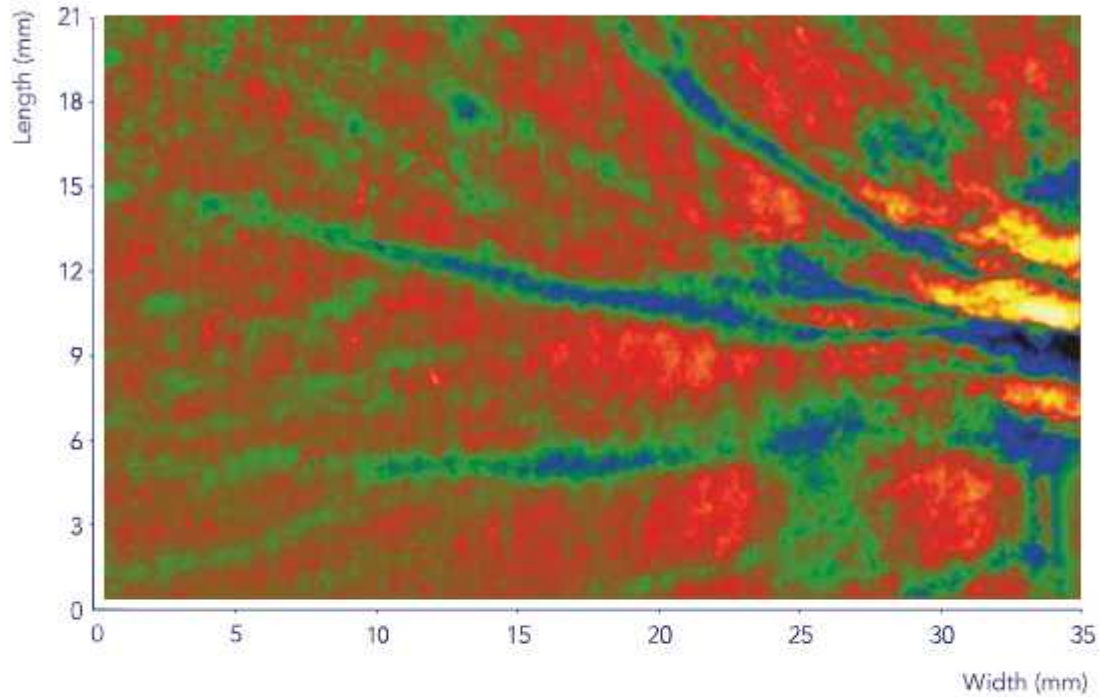
A STATISTICALLY SIGNIFICANT IMPROVEMENT IN
ELASTICITY AFTER ONLY TWO WEEKS OF TREATMENT.

A STATISTICALLY SIGNIFICANT REDUCTION IN WRINKLE
DEPTH: **10% AFTER ONLY TWO WEEKS AND
30% AFTER THREE MONTHS OF TREATMENT.**

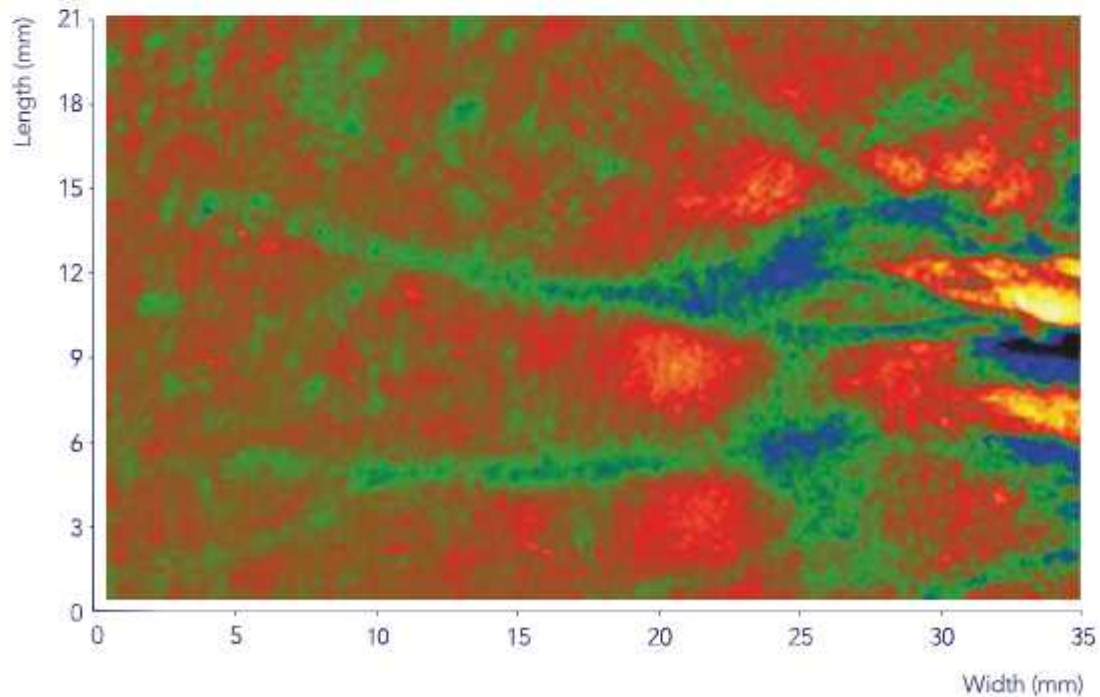
DERMATOLOGICALLY TESTED ON SENSITIVE SKIN.
NON-IRRITATING.

VISIBLE WRINKLES DEPTH REDUCTION IN THE PERIOCULAR AREA

Starting point



On the 84th day



Images taken with Canfield Primos 3D. Blue color indicates greater wrinkle depth.

PROFHILO®

+

PROFHILO HAENKENIUM®

A NEW STANDARD FOR FACE AND NECK TREATMENT.



Tamper-evident
packaging system



IS A CLASS III MEDICAL DEVICE

Each box contains:

- 1 Pre-filled 2 ml syringe
- 1 Product leaflet
- 2 Terumo needles 29G TW 13 mm
- 2 Product traceability stickers

Each box contains:

- 1 Airless bottle
- 50 ml of antioxidant cream

hydroACTION ■■■■■■
liftACTION ■■■■□□
CROSS-LINKING ■■■■■■

CE 0373



Quality Made in Italy. Quality is achieved through attention to details; not always visible, but always essential. IBSA is unique in this vast market, owing to its complete control of the hyaluronic acid lifecycle; from the raw material production to the finished product. IBSA's wide range of dermoaesthetic products, Made in Italy, is adaptable to meet various patient needs, with the goal of biorejuvenation. The knowledge, ongoing scientific research, technological development and state-of-the-art production processes makes IBSA one of the leaders in hyaluronic acid production.

IBSA Farmaceutici Italia

S.r.l Via Martiri di Cefalonia 2 - 26900 Lodi - Italy

Alma is a global innovator of Laser, Light-based, Radio Frequency and Ultrasound solutions for the aesthetic and surgical markets. We enable practitioners to offer safe and effective procedures while allowing patients to benefit from state-of-the-art, clinically proven technologies and treatments.

Alma Medical Pvt. Ltd.

Unit No. 203, 2nd Floor, B Wing, Supreme Business Park, Supreme City, Powai, Mumbai - 400 076, Tel. : +91 22 42154600 / +91 22 42154700, www.almasasers.co.in, info@almasasers.co.in

References

- 1) Stellavato A. et al. 2016; PLoS One 11(10):e0163510.
- 2) Stellavato A. et al. 2017 Cell Physiol Biochem 2017; 44:1078-1092.
- 3) Prothilo leaflet.
- 4) D'Agostino A. et al. 2015; BMC Cell Biol 16:19.
- 5) Sundaram H. et al. 2016; Poster Presentation, American Society for Dermatologic Surgery (ASDS) Annual Meeting.
- 6) Sparavigna A. et al. 2016; Clin Cosmet Investig Dermatol 9:297-305.
- 7) Laurino C. et al. 2015; Eplasty 15:e46.
- 8) Rodriguez Abascal M et al. 2015; Eur Aesth Plast Surg J 2015; 5(2): 124-131.
- 9) Beatini A. et al. 2016; Aesthetic Medicine 2(2):45-51.
- 10) Alimonti A. et al. Identification of Salvia haenkei as gerosuppressant agent by using an integrated senescence-screening assay. Aging (Albany NY) 2016; 8(12):32223-36.
- 11) IBSA internal data on file 2018.



Material intended for medical practitioner's use only