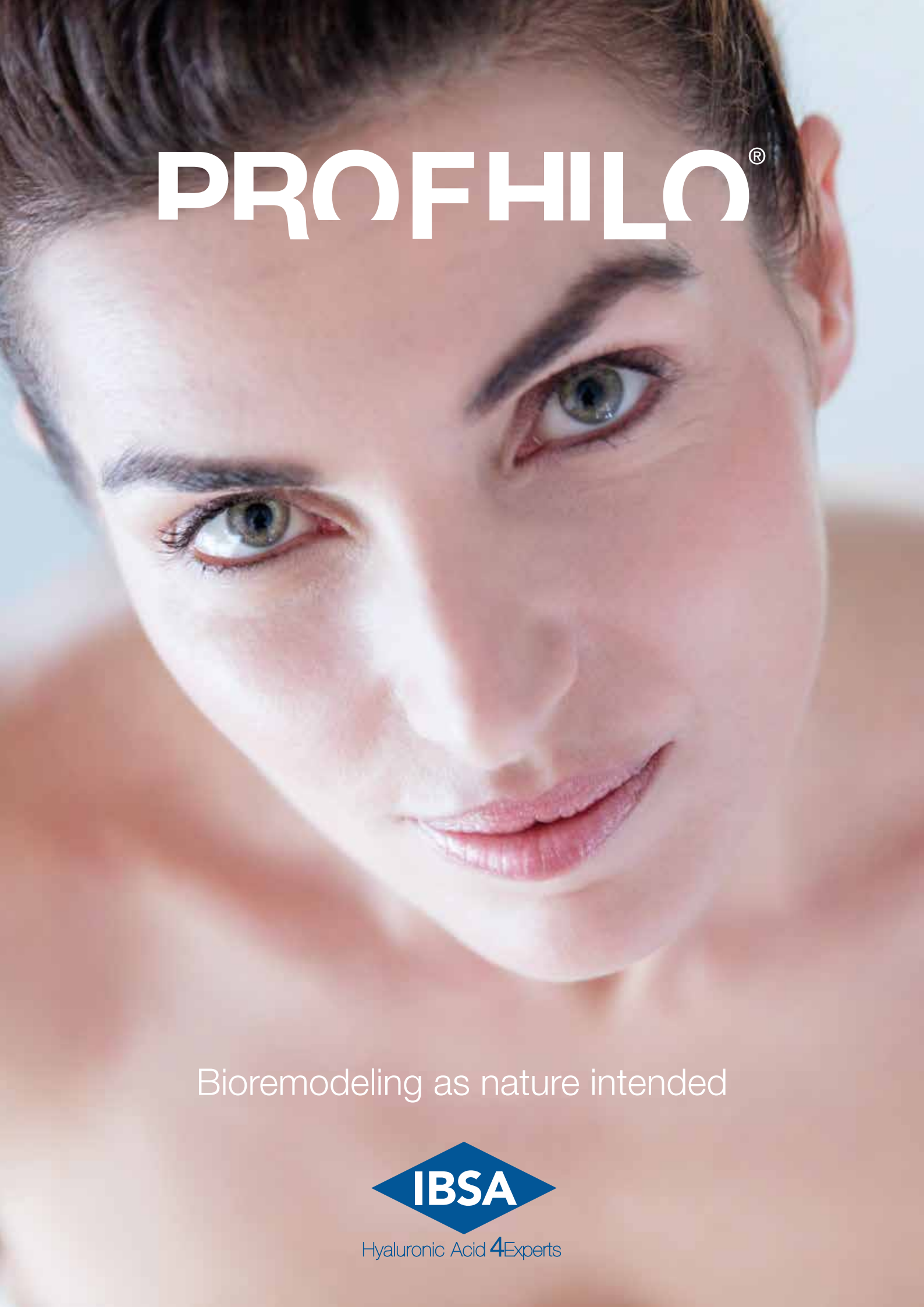

PROFHILO®
Bioremodeling as nature intended
IBSA
Hyaluronic Acid 4Experts

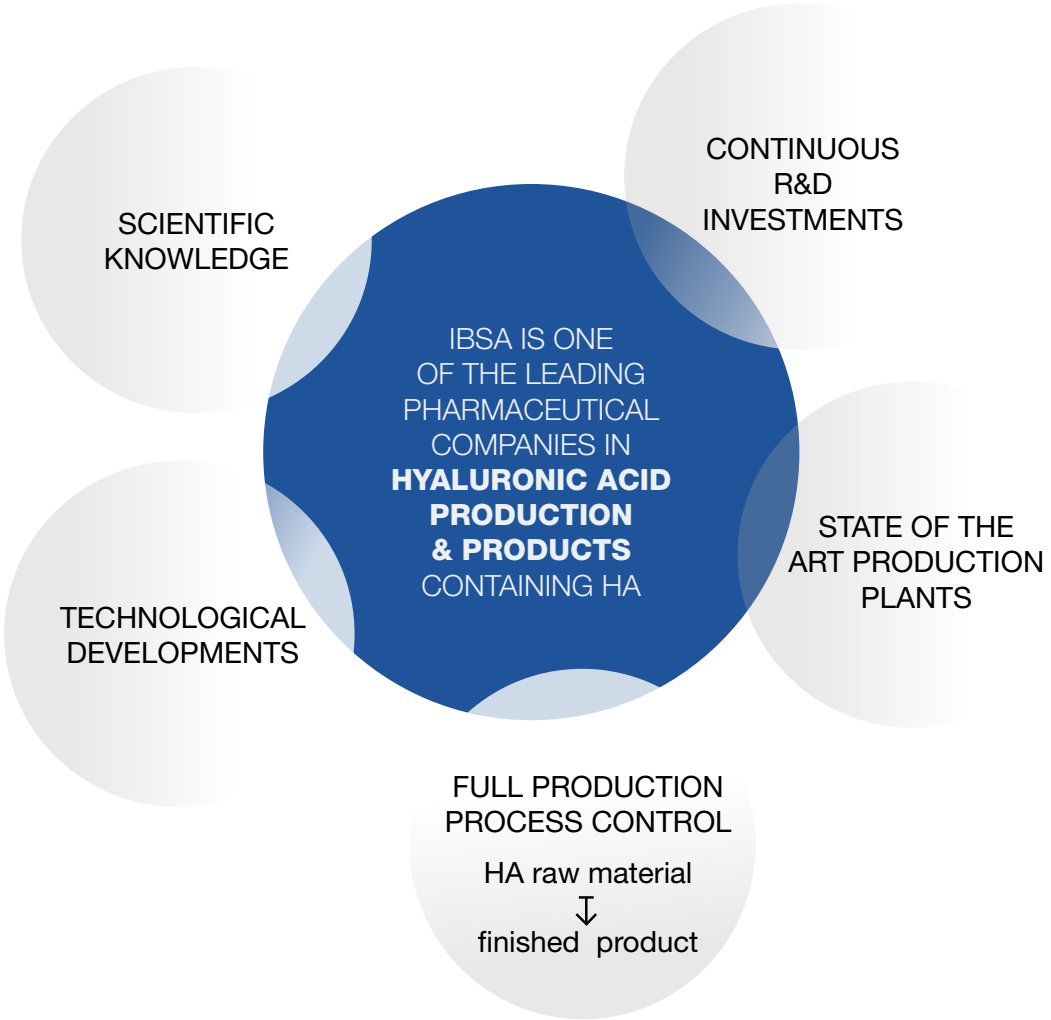
IBSA
Group

Institut Biochimique SA, founded in 1945, is the largest privately owned multinational pharmaceutical company in Switzerland.

*"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

OVER **25** OFFICES & MANUFACTURING PLANTS	HUNDREDS OF PRODUCTS COVERING **8** THERAPEUTIC AREAS	PRODUCTS AVAILABLE IN MORE THAN **80** COUNTRIES



The

DERMOAESTHETIC AREA

offers a full range of products and brands such as Viscoderm®, Profhilo® 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

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®
for BIOREMODELING

ITALIAN LAUNCH
February 2015

INTERNATIONAL LAUNCH
January 2016

150,000
treatments performed to date
December 2016

Available in
43 COUNTRIES by 2017

ANTI-AGING & BEAUTY TROPHY
3rd Anti-Aging & Beauty Trophy 2015-2016
Best Skin Enhancement Product
WINNER

AMEC & AESTHETICS AWARDS

WINNER 2016
Aesthetics Awards
THE BARRY KNAPP AWARD FOR PRODUCT INNOVATION OF THE YEAR

What's new

PROFHILO® STABILIZED HYBRID
COOPERATIVE COMPLEXES IS THE
FIRST PRODUCT DEVELOPED WITH

NAHYCO®
HYBRID TECHNOLOGY

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:

FIBROBLASTS[1] **KERATINOCYTES**[1] **ADIPOCYTES**[2]

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, for the malar and submalar areas,
the BAP (Bio Aesthetic Points) technique with only 5
injection points on each side of the face.

PROFHILO®

What's new

Production Process

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)

1

Thermal stabilization process

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

2

NAHYCO®
HYBRID TECHNOLOGY

Obtaining:

PROFHILO®

stabilized hybrid
cooperative complexes

3

A NEW TOOL with

UNIQUE CHARACTERISTICS:

- **High HA concentration** (64mg/2ml) [3]
- Highly manageable[4]
- Extensive spreadability[5]
- Low viscosity[4]
- **No BDDE** or other chemical agents[3]
- Low inflammatory response[4]
- Thermally stabilized **natural HA** with a duration comparable to a low cross-linked gel[5]

PROFHILO®

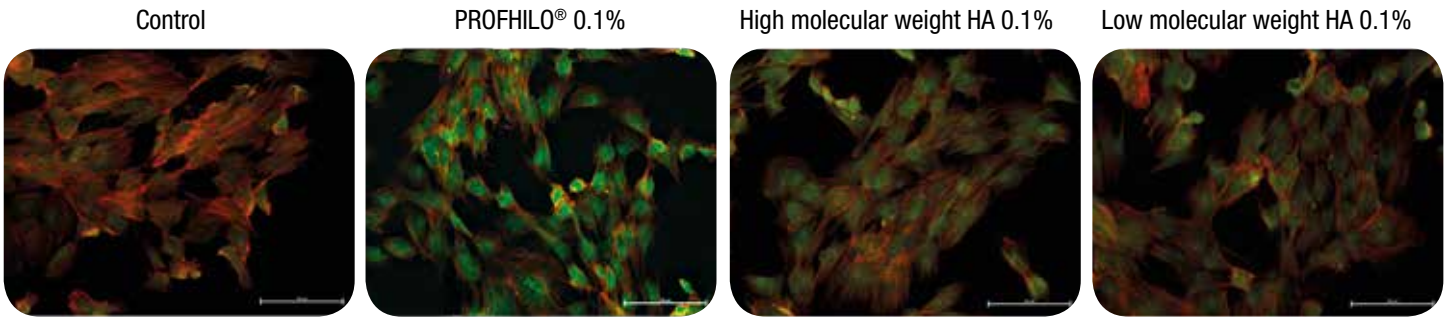
How it works

MULTI-LEVEL DYNAMIC REMODELING

In vitro studies have shown that PROFHILO® improves the extracellular environment:[1-2]

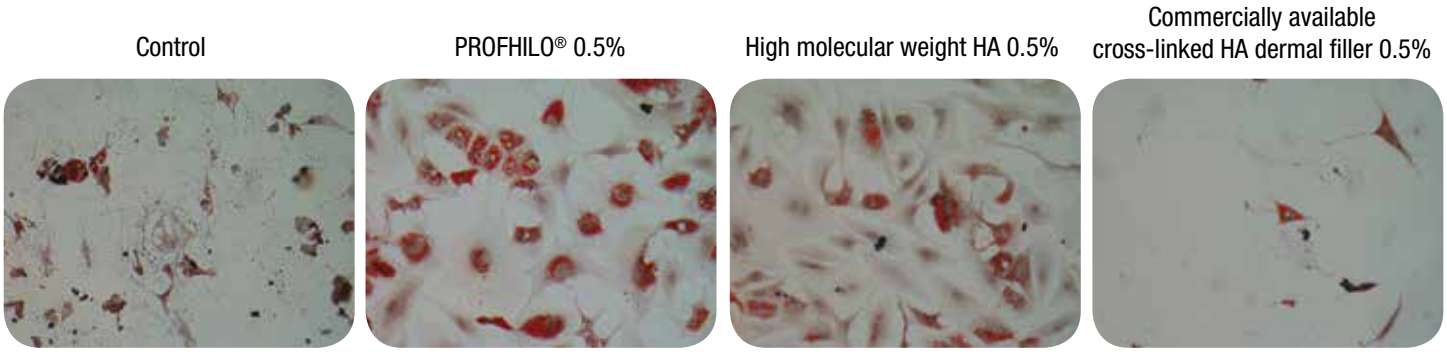
- **Maintaining suitable conditions for the viability of fibroblasts, keratinocytes and adipocytes.**
- **Leading to a remodeling of the extracellular matrix in terms of elasticity and support.**

PROFHILO® SUPPORTS FIBROBLAST VIABILITY



In vitro **elastin immunofluorescence staining on fibroblasts (Human Dermal Fibroblasts, HDF)[1]**

PROFHILO® SUPPORTS ADIPOCYTE VIABILITY



In vitro **Red Oil staining performed on Adipocyte Stem Cells in adipogenic medium, 14 days after incubation[2]**

PROFHILO® IN THE TISSUE

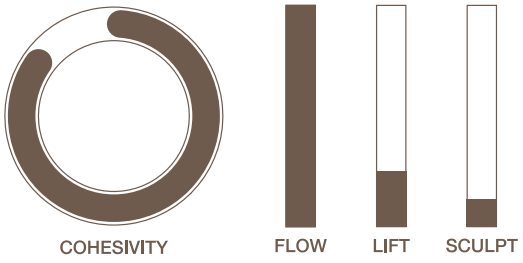
An important characteristic due to the high cohesivity of PROFHILO® is its **optimal tissue integration capacity.**[5]

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]

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 other cross-linked gels.[5]

The IBSA GPS Scale is based on actual rheological data:

GPS
GUIDE to PRODUCT SELECTION
SCALE



Adapted from Sundaram H, Cassuto D, Gavard Molliard S (publication submitted).

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

THANKS TO THE UNIQUE RHEOLOGICAL CHARACTERISTICS OF PROFHILO®, TISSUE **REMODELING IS EASILY OBTAINED IN ONLY 2 SESSIONS** *(4 WEEK INTERVAL)* USING ALL AESTHETIC INJECTION TECHNIQUES, IN THE SUPERFICIAL SUBCUTANEOUS LAYER.

REMODELING THE MALAR & SUBMALAR AREAS

After 150,000 successful treatments to date (Dec. 2016) and as published in literature[6-9], the **BAP** (Bio Aesthetic Points) **technique**, specifically developed for PROFHILO® by IBSA, is the most wide-spread, efficient and highly recommended protocol for treatment of the malar and submalar areas.

Preferred by patients:

★★★★★ Reduced number of treatment sessions

★★★★★ Reduced number of injection sites, therefore reduced discomfort per session

★★★★★ Reduced or eliminated downtime

PROFHILO®

How to use

THE BAP TECHNIQUE

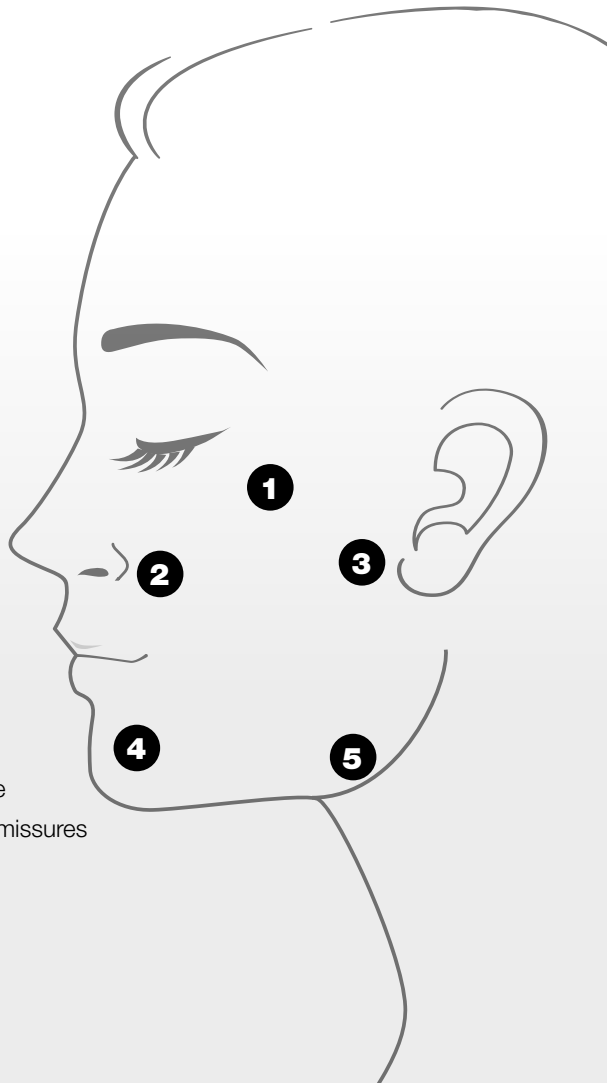
(BIO AESTHETIC POINTS)

This technique was created for the lower third of the face due to its predisposition to dermal atrophy caused by the aging phenomena.

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

inject 0.2 ml per bolus at the superficial subcutaneous layer

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.



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

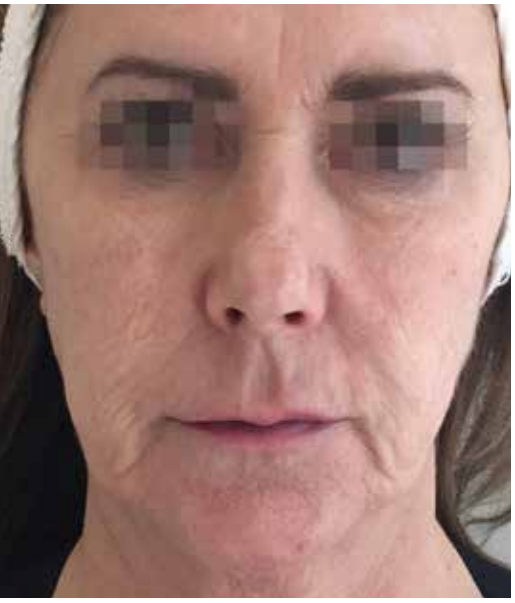
3 **TRAGUS**
1 cm anterior to the bottom of the tragus

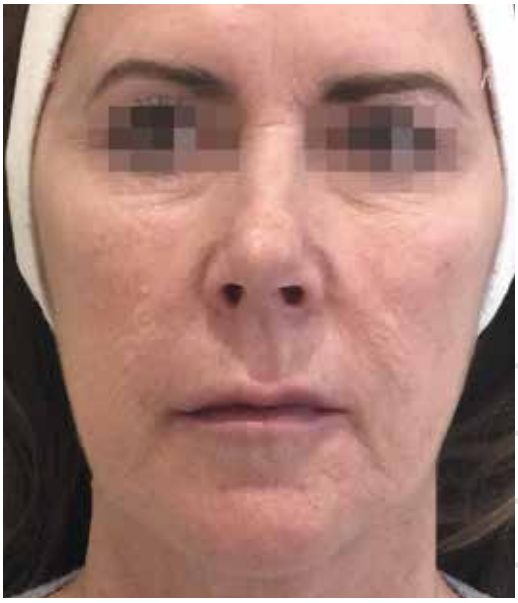
4 **CHIN**
- draw a vertical line in the center of the chin
- draw a perpendicular line one third from the top of the vertical line
- from the point of intersection move 1.5 cm towards the oral commissures

5 **MANDIBULAR ANGLE**
1 cm above the mandibular angle

PROFHILO®
Protocols

FACE

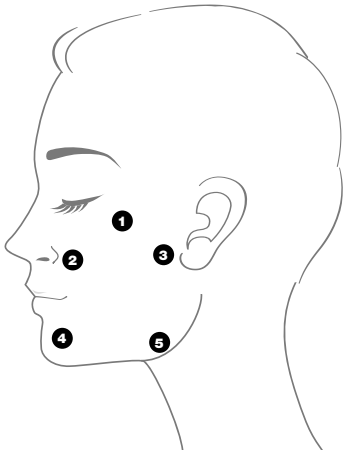




Baseline

1 month after 2nd treatment

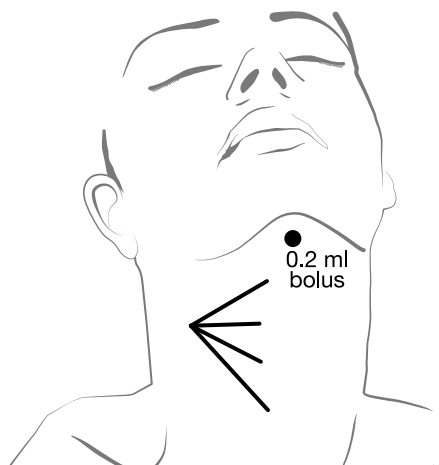
Courtesy of Dr. Emma Ravichandran
(Glasgow, Scotland)

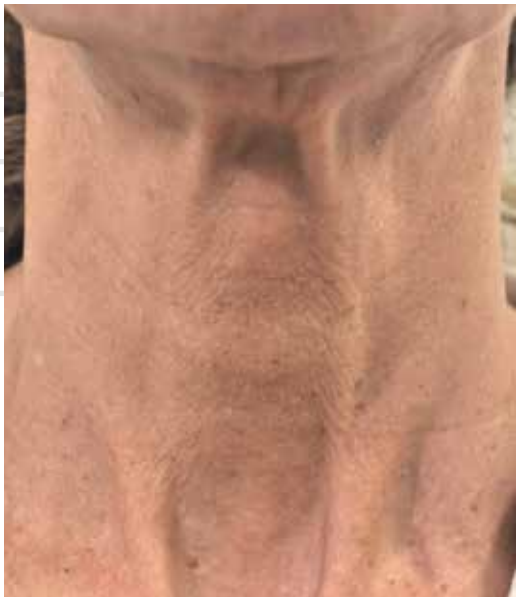


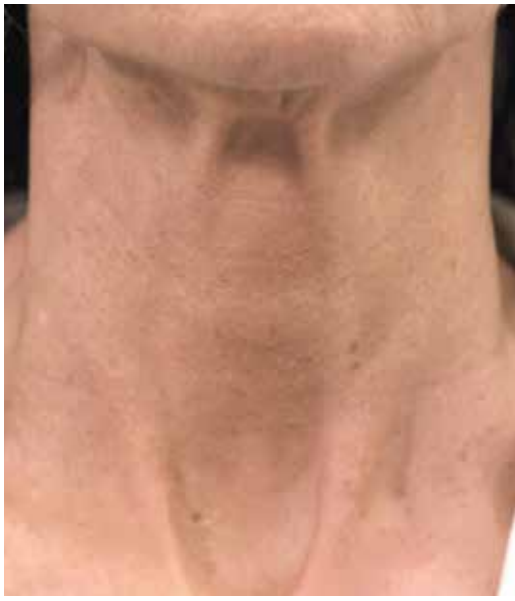
TECHNIQUE	BAP 29G 13 mm needle
PRODUCT QUANTITY	1 ml per side
TREATMENT SESSIONS	2 treatments
TREATMENT INTERVAL	4 weeks
FREQUENCY	twice per year

NECK

TECHNIQUE	1 bolus + fanning 29G 13 mm needle 25G 50mm cannula
PRODUCT QUANTITY	2 ml per side
TREATMENT SESSIONS	2 treatments
TREATMENT INTERVAL	4 weeks
FREQUENCY	twice per year





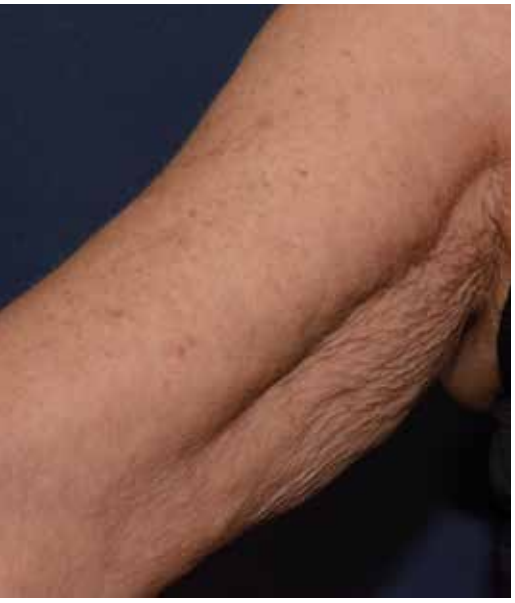


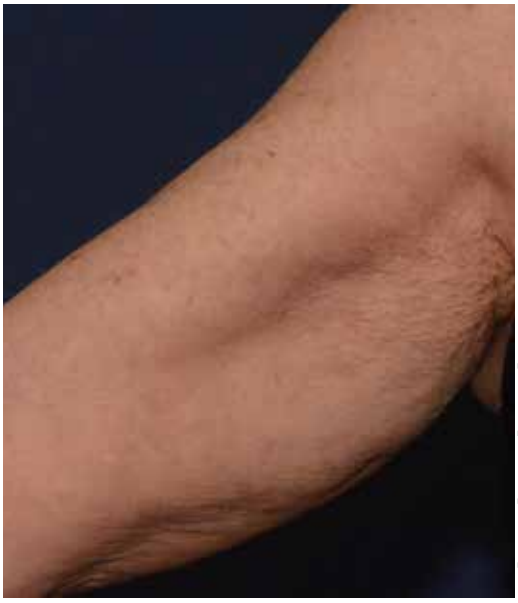
Baseline

1 month after 2nd treatment

Courtesy of Dr. Patrizia Piersini
(Turin, Italy)

INNER ARM

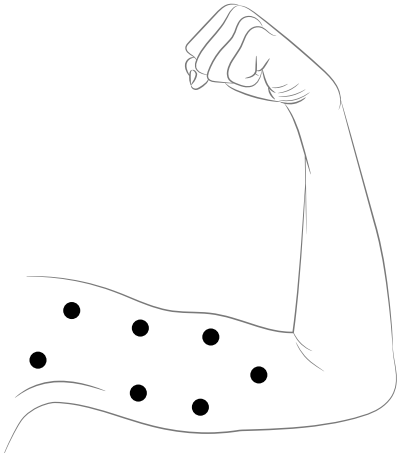




Baseline

1 month after 2nd treatment

Courtesy of Dr. Bruno Bovani
(Perugia, Italy)



TECHNIQUE	7 point technique 29G 13 mm needle
PRODUCT QUANTITY	2 ml per side (0.2-0.3 ml/bolus)
TREATMENT SESSIONS	2 treatments
TREATMENT INTERVAL	3 weeks
FREQUENCY	2-3 times per year

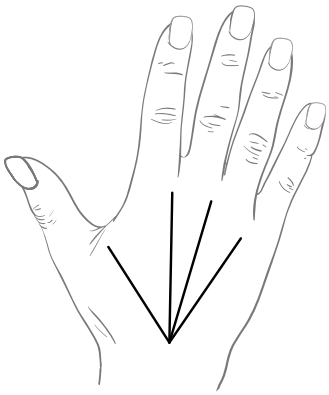
HANDS

TECHNIQUE	Fanning 25G 50 mm cannula
PRODUCT QUANTITY	2 ml per side
TREATMENT SESSIONS	2 treatments
TREATMENT INTERVAL	4 weeks
FREQUENCY	twice per year

Baseline

1 month after 2nd treatment

Courtesy of Dr. Giovanni Salti
(Florence, Italy)



PROFHILO®

Combined protocols

PROFHILO® **has significant potential for synergistic combination with conventionally cross-linked fillers to finesse volumetry results.[5]**

Aliaxin® + PROFHILO®

PRODUCT	Aliaxin® EV	PROFHILO®
TREATED AREA	Mandibular contour	Neck
TECHNIQUE	Fanning 22G 60 mm cannula	Fanning 25G 50 mm cannula
PRODUCT QUANTITY	1 ml per side	2 ml per side
TREATMENT SESSIONS	1 treatment	2 treatments
TREATMENT INTERVAL	4 weeks for touch-up if necessary	4 weeks
FREQUENCY	twice per year if necessary	twice per year

REDEFINITION OF MANDIBULAR CONTOUR AND NECK REMODELING

Baseline

1 month after 2nd treatment

Courtesy of Prof. Daniel Cassuto (Milan, Italy) and Dr. Irfan Mian (London, UK)

PRODUCT	Aliaxin® GP	PROFHILO®
TREATED AREA	Cheekbones	Malar - Submalar
TECHNIQUE	Bolus deep on bone 27G 19 mm needle	BAP 29G 13 mm needle
PRODUCT QUANTITY	1 ml per side	1 ml per side
TREATMENT SESSIONS	1 treatment	2 treatments
TREATMENT INTERVAL	4 weeks for touch-up if necessary	4 weeks
FREQUENCY	twice per year if necessary	twice per year

Baseline

1 month after 2nd treatment

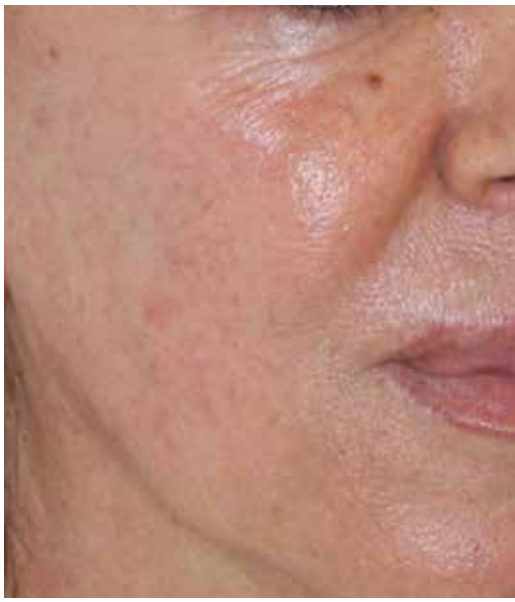
Courtesy of Dr. Sharon Davidson (Tel Aviv, Israel)

FACIAL REMODELING AND CHEEKBONE ENHANCEMENT

RESTORING SUBCUTANEOUS TISSUE DISORDERS

PROFHILO® treatments with cannula for subcutaneous recovery improve the quality of this layer, thus preparing the tissue for treatments with ALIAXIN®.

Baseline



1 month after 2nd treatment

Courtesy of Prof. Daniel Cassuto (Milan, Italy)

PROFHILO®

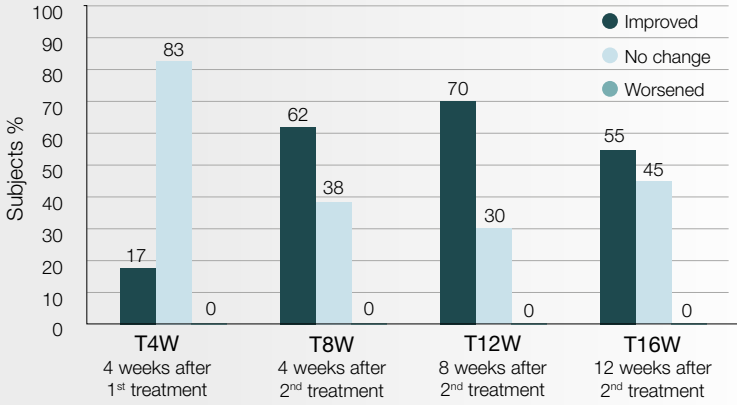
Results

PROFHILO®'s tightening action has a positive effect on facial volume [6]

Evaluation on 64 female patients treated using BAP technique

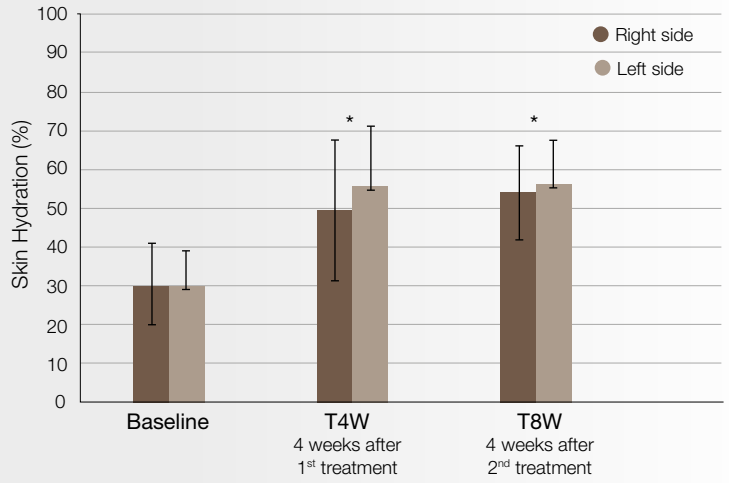
Average age 53 yrs (Range 38-60 yrs)

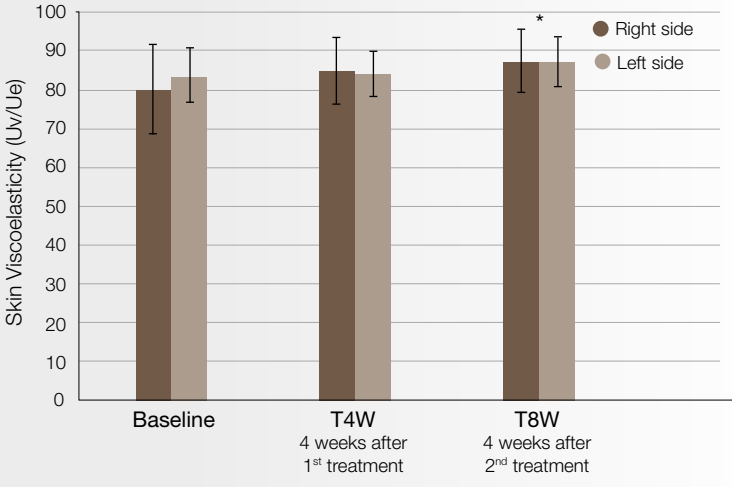
FVLS (Facial Volume Loss Scale range 2-3)



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

Improved hydration and elasticity [9]





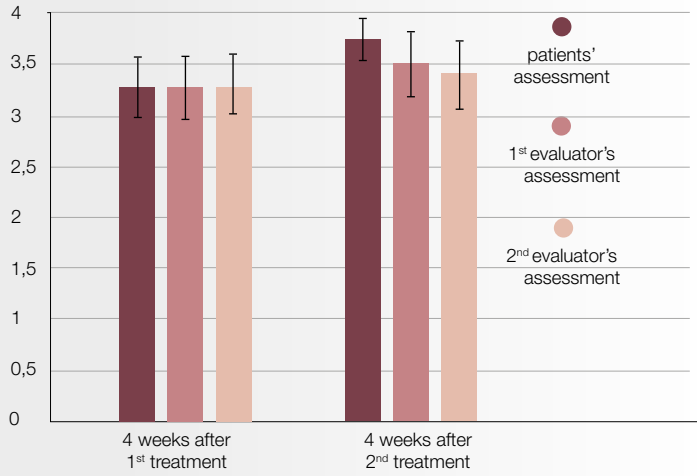
Evaluation on 15 female patients treated using BAP technique

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

High satisfaction of doctors and patients [8]



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 outcome.[5]**

Based on these characterizations, PROFHILO® **represents an intriguing new paradigm for skin restoration and improvement of skin laxity.[5]**

PROFHILO® **has significant potential for synergistic combination with conventionally cross-linked fillers to finesse volumetry results.[5]**

PROFHILO®

In vitro and clinical studies

BMC Cell Biol 2015;16:19.

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. 2015.
BMC Cell Biol 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

PubMed

PLoS One 2016;11(10):e0163510.

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

Stellavato A. et al. 2016.
PLoS One11(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 complex[38]. […]

Full text available on PubMed, PMID: 27723763

PubMed

Eplasty 2015;15:e46.

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

Laurino C. et al. 2015.
Eplasty 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 biorevitalizing 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 staminal 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. […]

Full text available on PubMed, PMID: 26491508

PubMed

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

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

Rodriguez Abascal M. et al. 2015.
Eur Aesth Plast Surg J 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. […]

Clin Cosmet Investig
Dermatol 2016;9:297-305.

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. 2016.
Clin Cosmet Investig Dermatol 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 WSRS score, profilometric, torsiometric, and skin electrical capacitance parameters. These instrumental and clinical findings are also confirmed by the photographic documentation. […]

Full text available on PubMed, PMID: 27713647

Aesthetic Medicine
2016;2(2)

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

Beatini A. et al. 2016.
Aesthetic Medicine 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. […]

*Summaries were extracted from the studies.

PROFHILO® IS A MEDICAL DEVICE CLASS III,
AVAILABLE IN A 2 ML READY TO USE, STERILE, PRE-FILLED
GLASS SYRINGE WITH 2 NEEDLES.

CE 0373

Tamper-evident packaging system

Each box contains:

1 Pre-filled 2 ml syringe

1 Product leaflet

2 Terumo needles 29G TW 13 mm

2 Product traceability stickers

hydro*ACTION* ●●●●●
lift*ACTION* ●●●○○
CROSS-LINKING □□□□□

ibsaderma.com
info@ibsaderma.com

IBSA
Hyaluronic Acid 4Experts

4me.style
ibsa derma

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

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1) Stellavato A. et al. 2016; PLoS One 11(10):e0163510.
2) Prof. Papaccio & Prof. Schiraldi's Research group internal data.
3) Profhilo 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) Rodríguez 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.

Vers. 2