PROFHILO®

Bioremodeling
as nature intended

Alma
For You. For Life.

IBSA
Caring Innovation

WHEN TWO GIANTS MEET, THE OUTCOME IS REMARKABLE

IBSA and Alma are teaming up to bring the-best-of-the-west-to-the-east!

IBSA - Institut Biochimique SA, founded in 1945, the largest privately owned multinational pharmaceutical company in Switzerland, and Alma - A world leading provider of energy based solutions for the surgical, medical aesthetics and beauty markets, founded in 1999, one of the top 5 global leaders in the industry and number 1 in the PRC, are joining forces to bring the novel, award-winning, Bioremodeling filler to the Asia Pacific markets.

IBSA
Group

Scientific knowledge, continued research, technological development and modern production processes, make IBSA one of the leading phar-maceutical companies in hyaluronic acid production. IBSA, in fact, distinguish itself in the vast dermoesthetic market because it controls the entire product life cycle, from the biofermentation raw material production to the finished product in pre-filled syringes.

- ONE OF THE WORLD LEADERS IN HYALURONIC ACID-BASED SOLUTION
- THE LARGEST PRIVATE PHARMACEUTICAL COMPANY IN SWITZERLAND WITH 25 FACTORIES & LABORATORIES IN SWITZERLAND, ITALY & CHINA
- PRODUCTS AVAILABLE IN MORE THAN 80 COUNTRIES IN 5 CONTINENTS

Alma™

A world-leading provider of energy-based solutions for the surgical, medial aesthetics and beauty markets, with solid track record since October 1999.

- ONE OF THE TOP 5 GLOBAL INDUSTRY LEADERS
- #1 IN THE PEOPLE'S REPUBLIC OF CHINA!
- WORLDWIDE SALES NETWORK ACROSS 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

Over
400,000
treatments performed
September 2018

Available in
56 COUNTRIES by end of 2018

BEST PRODUCT AWARDS
2016-2018

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

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

THE Aesthetic Industry Awards
Aesthetic Winner 2018
THE Aesthetic Guide

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

PROFHILO®

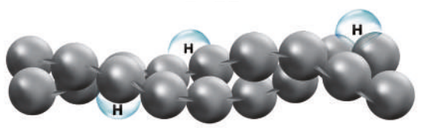
What's new

Production Process

1 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)

HI



+

LO

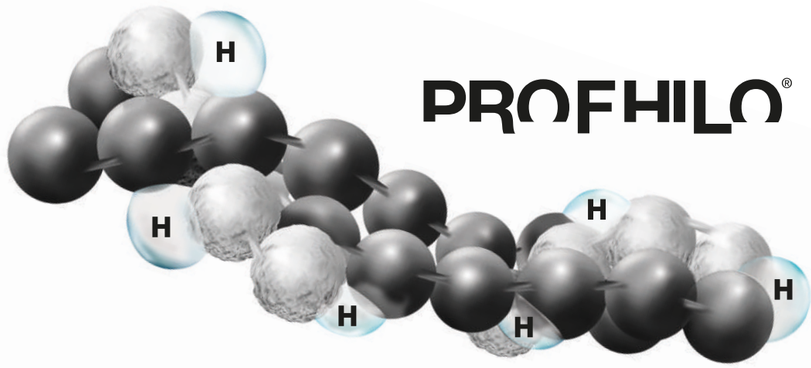
2 Thermal stabilization process

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

NAHYCO®
HYBRID TECHNOLOGY

3 Obtaining: PROFHILO®

stabilized hybrid
cooperative complexes



PROFHILO®

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]

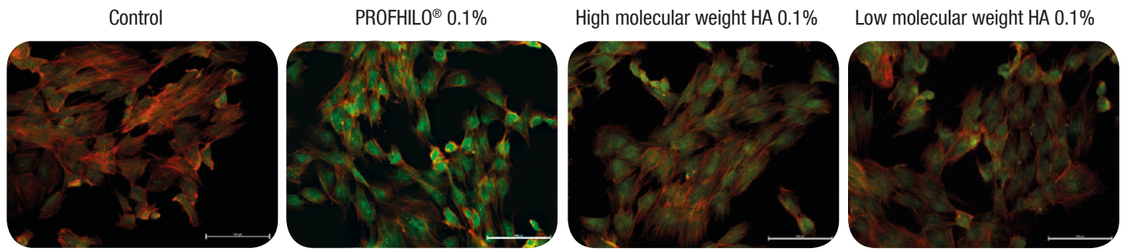
PROFHILO®
How it works

MULTI-LEVEL DYNAMIC REMODELING

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

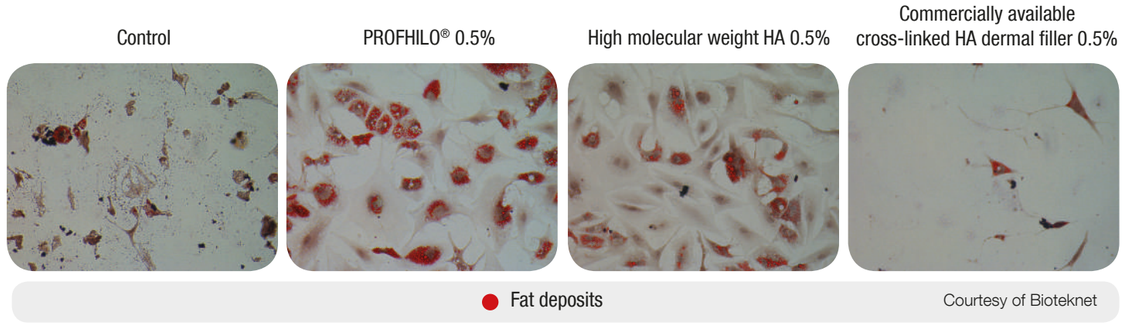
- **Maintaining suitable conditions for the viability of fibroblasts, keratinocytes and adipocytes.**
- **Leading to a remodeling of the extracellular matrix in terms of elasticity and support.**

KERATINOCYTES-FIBROBLASTS: PROFHILO® INCREASES ELASTIN EXPRESSION

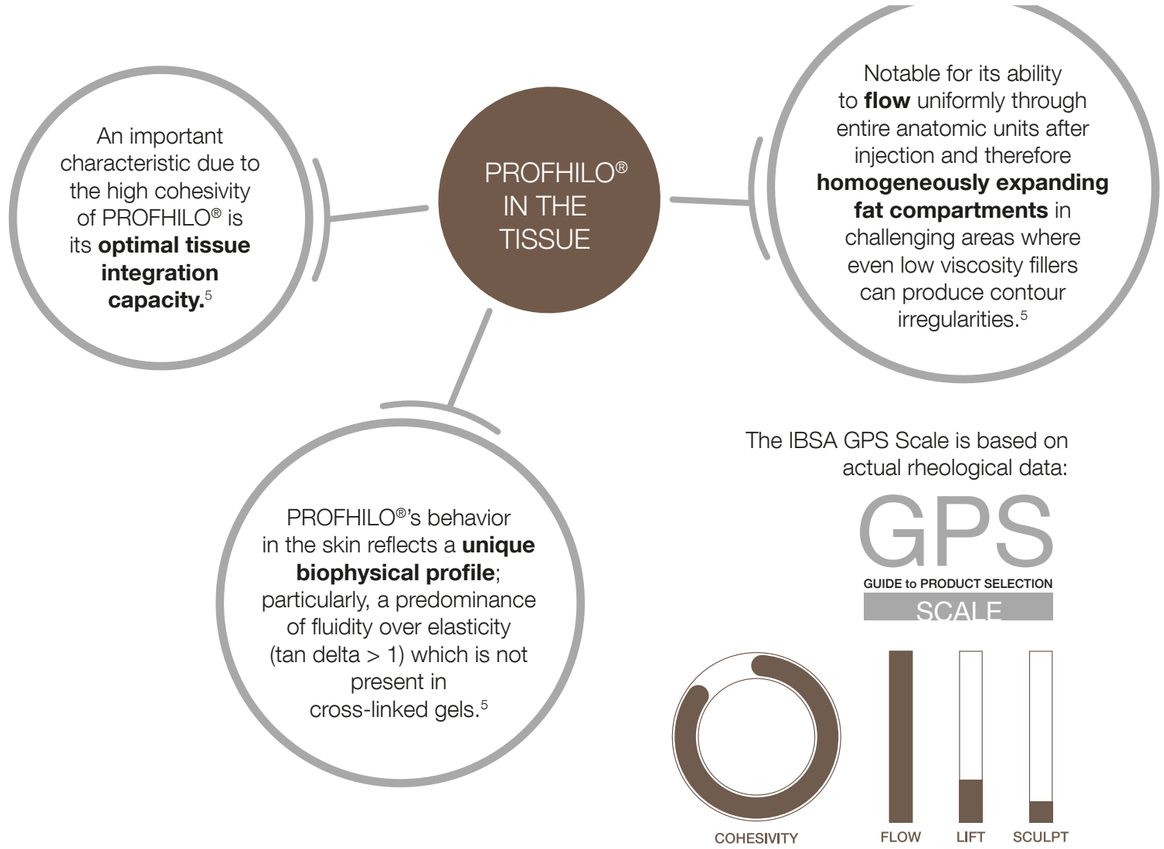


In vitro keratinocytes-fibroblasts immunofluorescence pictures relative to elastin expression[1]

ADIPOCYTES: PROFHILO® SUPPORTS VIABILITY



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



The IBSA GPS Scale is based on actual rheological data:

GPS
GUIDE to PRODUCT SELECTION SCALE

Adapted with permission from: Sundaram H, Cassuto D, Gavard Molliard 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 areas[6-9].
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.

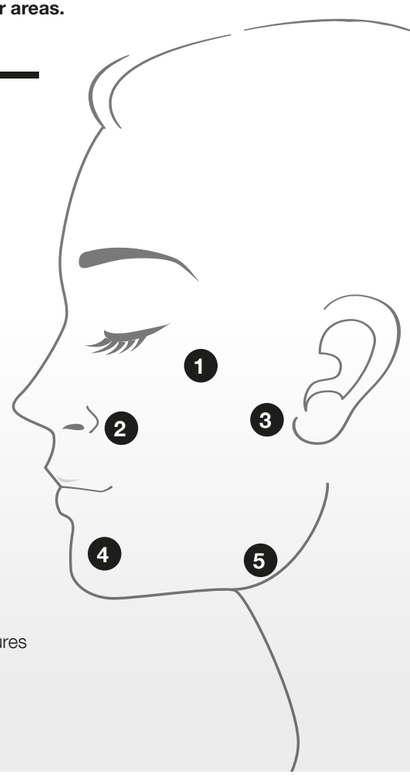
REMODELING THE MALAR & SUBMALAR AREAS

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



NECK REMODELING

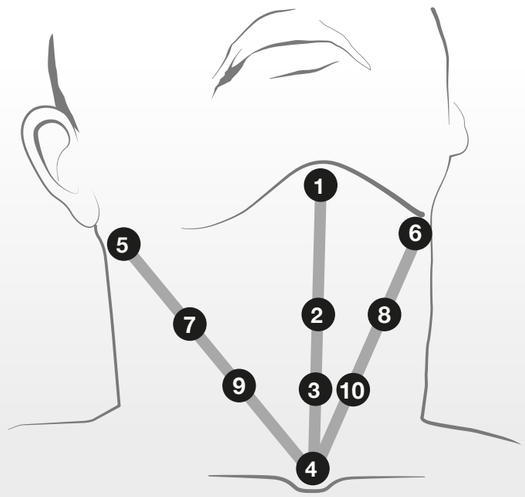
The 10 point BAP Neck Technique was developed in order to: provide reproducible points of injection, standardize these points irrespective of variations between patients and ensure that the injection points avoid potential injury to vital structures.

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. 6. Horizontal line with mandibular angle & 0.5 cm lateral to medial border of the SCM
7. 8. Horizontal line between apex of Adam's Apple and bottom of thyroid cartilage
9. 10. Horizontal line between the base of thyroid cartilage and sternal notch



Preferred by patients:

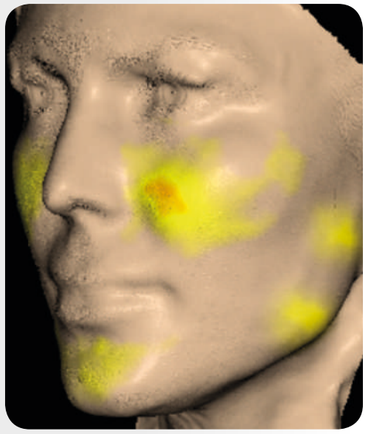
★★★★★ Reduced number of treatment sessions

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

★★★★★ Reduced or eliminated downtime

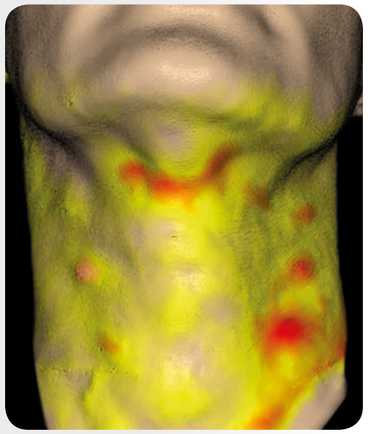
*Number of treatments and product quantity depend on the degree of aging.

PROFHILO® FLOWABILITY EVIDENCE BASED PERSPECTIVE



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

- 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.

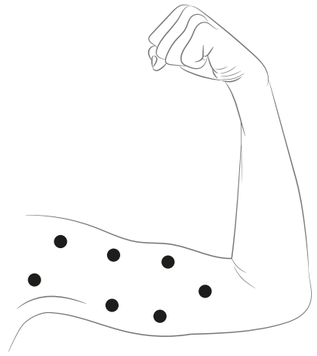


Images taken with 3D LIFEVIZ® mini camera from Quantificare

PROFHILO® Protocols

BAP FACE TREATMENT

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



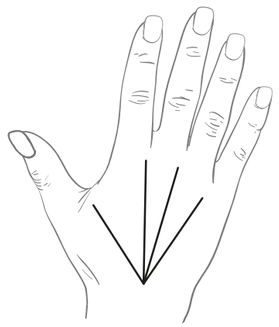
TECHNIQUE	7 point technique 29G 13 mm needle
PRODUCT QUANTITY	2 ml per arm (0.2-0.3 ml/bolus)
TREATMENT SESSIONS	2 treatments
TREATMENT INTERVAL	3 weeks
FREQUENCY	2-3 times per year

INNER ARMS

BAP NECK TREATMENT

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

TECHNIQUE	Fanning 25G 50 mm cannula
PRODUCT QUANTITY	2 ml per hand
TREATMENT SESSIONS	2 treatments (1 month interval)
FREQUENCY	twice per year



HANDS

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

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)

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

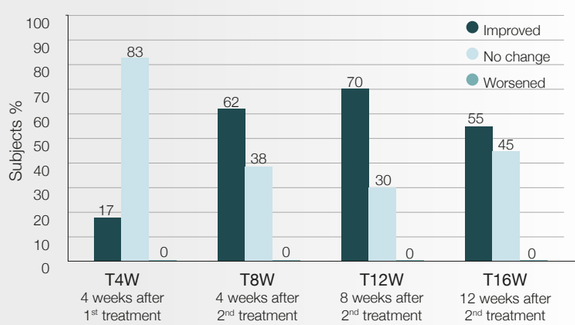
RESTORING SUBCUTANEOUS TISSUE DISORDERS

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®'s tightening action has a positive effect on facial



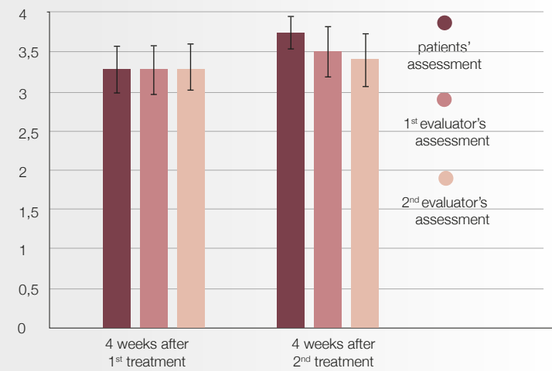
Evaluation on 64 female patients treated using BAP technique

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

High satisfaction of doctors and patients [8]

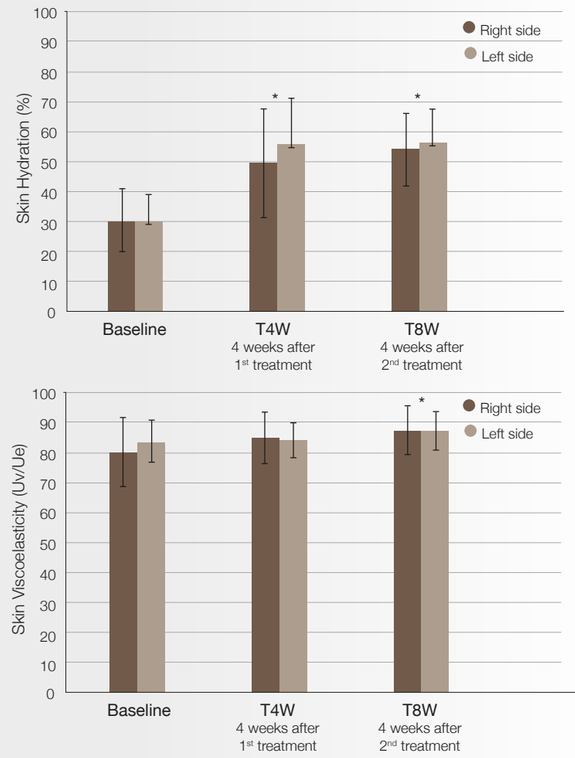


Evaluation on 30 female patients treated using BAP technique

Average age 53 yrs (Range 40-68 yrs)

Significant improvement of satisfaction levels after the second treatment

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

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

D'Agostino A. et al.

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

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

Stellavato A. et al.

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

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 complex[38]. […]

Full text available on PubMed, PMID: 27723763

Stellavato A. et al.

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

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

Laurino C. et al.

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

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 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

Rodriguez Abascal M. et al.

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

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. […]

Sparavigna A. et al.

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

Clin Cosmet Investig 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 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

Beatini A. et al.

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

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. […]

*Summaries were extracted from the studies.

IBSA
Caring Innovation

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.

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Alma
For You. For Life.

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.

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info@almalasers.com

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) 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.

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PBIB28101801