

COSMETIC MEDICINE + AESTHETIC SURGERY

1.25

.....
**THE FLYING WING
EXCISION – THE DIRECT
BROWLIFT FOR MEN**
.....

**A NARRATIVE REVIEW
ON CONTOURING THE CHIN
AND LOWER JAWLINE
WITH FILLER INJECTIONS**
.....

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HYBRID FILLERS
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WHAT DO WE KNOW
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.....

**FILLER
GUIDE
2025**

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The future is bright!

Aesthetic Medicine (AM) is a growing subspecialty of medicine. The increase of the number of minimal-invasive aesthetic procedures during the last decades is stunning. The power of innovation has been the fuel of development. By the introduction of new technologies and combination of established procedures a broad range of personalized medicine has become available.

AM is facing challenges. It cannot be a substitute of honest classic medicine dealing with prevention and treatment of diseases. However, it can be a very useful adjunct to classic medicine. A good example is reconstructive surgery, where both surgery and aesthetics are entwined. Combating the signs and symptoms of aging skin has the potential to prevent precancerous lesions. Considering actinic keratoses, tools of AM such as peeling can be used therapeutically.

Current challenges within the field of AM include a lack of global standards for the education of AM specialists, the spread of AM being practiced outside by lay persons, and the overwhelming influence of social media [1].

Responsibility and safety are important issues. Standardized education on a high scientific level was a major aim of the German Society of Botulinum Therapy (DGBT) from its very beginning. Detailed knowledge of anatomy, physiology, pharmacology combined with practical training courses are the backbone of its success. We need to be critical considering our own concepts and skills. To ensure patient safety, an open-minded, honest analysis of adverse events and the interdisciplinary development of treatment guidelines and algorithms in cases of unwanted side effects are most helpful for patients and doctors. This is the major task of the International Society for Aesthetic Competence (ISAC). In the present issue of COSMETIC MEDICINE + AESTHETIC SURGERY Tanja Fischer (president of ISAC) and Said Hilton (president of DGBT) explained the fruitful cooperation of both societies: "The DGBT is a pioneer in training, while ISAC specializes in safety concepts and emergency management. Together, we can create international standards that give doctors more security and protect patients." Similar projects are underway in other countries.

AM is at a turning point. While enhancement of appearance was the primary impetus of AM for centuries, preservation and regeneration of tissues has become reality. Translational medicine is part of AM and AM is part of translational medicine. The integration of artificial intelligence just started. AM must navigate "the delicate balance between harmony and hype, ensuring that the pursuit of innovation does not compromise scientific integrity or ethical standards" [2].

The future of Aesthetic Medicine will be bright if we carefully respond the challenges if we practice it skillfully, consistently, and thoughtfully.

Enjoy the current issue of the journal!

Uwe Wollina, Dresden



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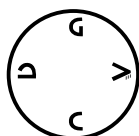
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MY·FILLER



New Life to the Skin

HA dermal fillers and 2nd generation skinboosters.

A narrative review on contouring the chin and lower jawline with filler injections

UWE WOLLINA

KEYWORDS:

facial aging, anatomy, filler, sagging cheeks, chin

SUMMARY:

The lower third of the face plays an important role in facial ageing. Changes in the ligaments and retinaculæ cutis, the dermal connective tissue and the fat compartments lead to the formation of so-called sagging cheeks and to aesthetically disturbing modifications of the chin region. The anatomical basis and general information on filler injections are supplemented by an overview of published filler studies. Safety aspects and limitations of the studies are discussed.

- Studies in English or German;
- Information on fillers and injection techniques;
- Performed on healthy adults;
- Data access.

Exclusion criteria were:

Studies on fillers in other indications and outside the lower third of the face. The search was carried out using the following keywords: *Filler, Face, Aging, Esthetics, Jawline, Chin, Marionette Lines* and *Trial*. *Filler AND Trial* yielded 1008 studies, *Filler AND Face AND Trial* yielded 362 hits. *Filler AND Face AND Trial AND Esthetics* yielded 215 studies, *Filler AND Jawline* yielded 71 studies and *Filler AND Chin* yielded 123 studies. *Filler trial AND Chin* yielded 12 studies, *Filler trial AND Marionette lines* 11 and *Filler trial AND Jawline* 6 publications.

INTRODUCTION

The lower third of the face cannot be ignored as part of the facial ageing process. The following factors play a decisive role:

- Sagging of the skin and connective tissue in the cheek area and perioral region.
- Malar fat tissue reduction.
- The resorption of bone in the upper and lower jaw.
- The position of the teeth, possible tooth loss, dentures.

As a result of these processes, there is a successive reduction in the definition of the mandibular line (jowls) and surface irregularities of the chin region such as dimpled chin and chin ptosis, perioral radial wrinkles and emphasis of the mandibular crease. In this review, we focus on the chin and mandibular line. With regard to dynamic perioral wrinkles, please refer to the reviews [1–3].

MATERIAL AND METHODS

A literature search of the years 2010–2024 was conducted via PUBMED. Inclusion criteria were:

ANATOMY AND AGING

Jowls (“sagging cheeks”): There are various hypotheses regarding their origin. Mendelson et al. described the jowls as changes in the sub-platysmal, deep tissue layer [4]. In contrast, Reece & Rohrich assumed a supra-platysmal location [5]. More recent studies by Minelli et al. (2023) were able to confirm that the jowls are supra-platysmal [6].

The area in which the jowls develop are zones of maximum sliding of the subcutaneous tissue layers over the musculature during mandibular movements. The retinacula cutis, which connect the skin to the muscles above the mandibular ligaments, are significantly longer than in other supra-platysmal areas. With increasing age, the connective tissue fibers lose elasticity and become longer.

The age-related changes take place in several stages:

- In patients with thin skin and minimal jowl formation, there is atrophy of the subcutaneous fatty tissue.
- Cheek ptosis with normal skin, loss of the sub-malar depression and tissue fullness in the midface is caused by caudal displacement of fatty tissue compartments.

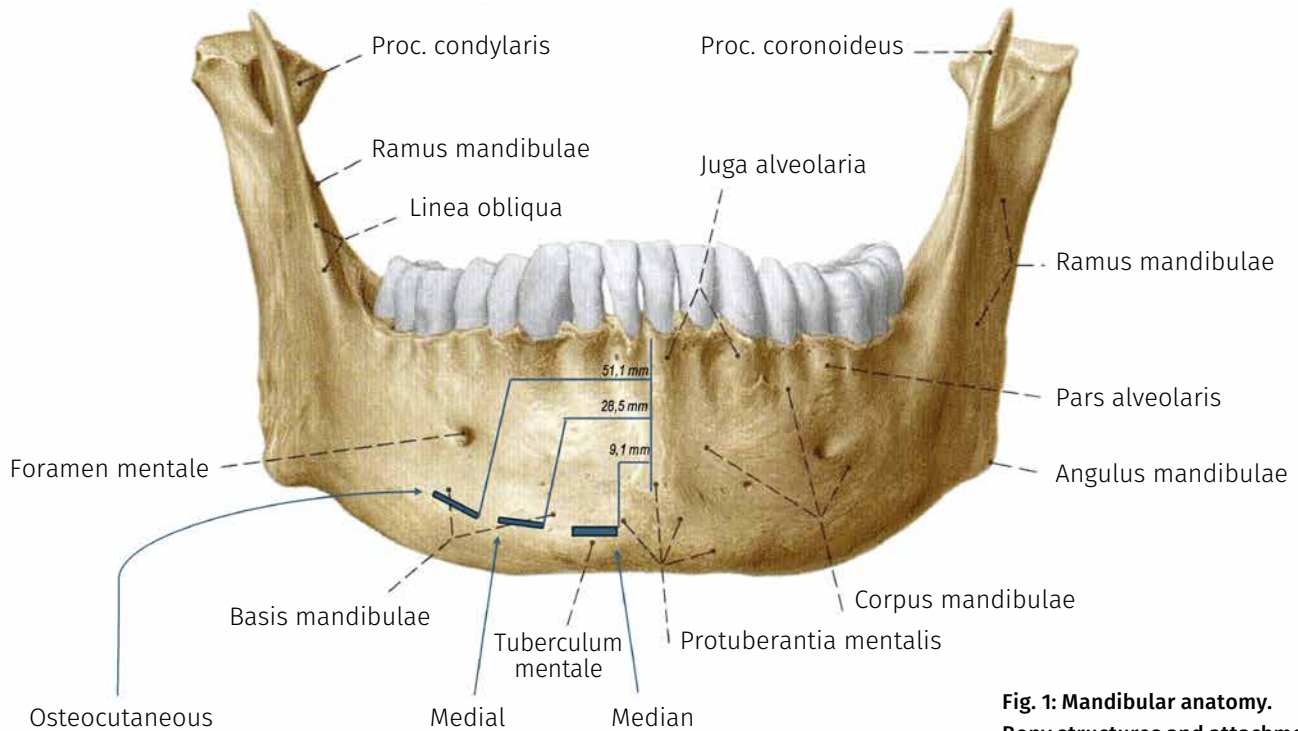


Fig. 1: Mandibular anatomy. Bony structures and attachments of the ligaments (L.) modified after Kang et al. (2016).

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- Cascading, confluent fatty tissue over the mandible is caused by septal dehiscence.

There are 3 retaining ligaments on the chin according to Kang et al. (2016) (Fig. 1). They are located in the sub-platysmal layer:

- The mental ligament lies ca. 9 mm lateral to the midline and 8.4 mm above the lower edge of the mandible.
- The medial mandibular ligament, which is located almost 29 mm lateral to the midline and slightly more than 8 mm superior to the lower edge of the mandible.
- The mandibular osteocutaneous ligament, more than 50 mm lateral to the midline and approximately 9 mm above the lower edge of the mandible [7].

According to recent anatomical studies, the mandibular ligament lies posterior to the jowl formation. The maximum caudal extension of the jowls is positioned over the posterior border of the medial mandibular ligament. The ligaments are not directly involved in the anterior and posterior borders of the jowls [6].

Mandibular fold: The labiomental or mandibular fold (“marionette line”) is formed by direct insertion of fibers of the orbicularis oris muscle and the “tectonic” transition zone of the SMAS (superficial musculoaponeurotic system) from type I (cheek) to type II (lips).

SMAS type I consists of parallel fibrous septa that connect the mimic musculature with the skin, while type II has stronger fasciae and smaller fatty tissue components [8]. The genesis of the mandibular fold is thus analogous to the nasolabial fold [6].

The mental fold is located between the lower lip and the prominence of the chin. It is created by contraction of the mentalis muscle [9].

The chin derives its shape from the bony structures, especially the symphysis, and the overlying soft tissue. Three-dimensional tomography and cadaver dissections indicate a significantly stronger vascularization of the superficial soft tissues than the deep parts [10]. This is important for esthetic filler injections.

Chin ptosis is caused by displacement of soft tissue from the symphysis of the mandible over the caudal edge of the mandible [11]. It can be dynamic, i.e. caused by muscular activity. These patients have a horizontal smile.

In “illusory chin ptosis”, the lip position and the intra-oral sulcus are normal, as are the mimic movements. This type is caused by a pronounced submental crease, which can also sometimes exceed the lower edge of the mandible towards the head. Smiling does not change the perceived “ptosis”. In addition, there are variants that occur due to morphogenetic disorders or postoperatively.

These changes are primarily corrected surgically and will therefore not be considered further here [12].

Dimpled chin is caused by contractions of the mentalis muscle and occurs as a dynamic phenomenon, particularly during speech [13]. Because of this mimic component, treatment with botulinum toxin is a priority [2].

Subcutaneous fatty tissue: Subcutaneous fatty tissue is involved in the development of the jowls and the mandibular fold. This is not present as a uniform layer but is structured in various compartments with stratification into deep and superficial parts.

Regarding the jowls, the lateral-temporal cheek compartment, the middle cheek compartment, the labio-mandibular compartment and the jowl compartment under the middle cheek compartment are of interest. The labiomandibular compartment plays the dominant role in mandibular folds. For the dimpled chin, the chin compartment is of interest [14]. The structural and pathophysiological changes of the subcutaneous adipose tissue are of great relevance for the aging process of the face [15].

FILLER FOR AESTHETIC APPLICATION IN THE LOWER THIRD OF THE FACE

In the following, we provide an overview of the published studies on filler treatment of the jowls, chin and mental folds, which are of outstanding importance for the aesthetics of the lower third of the face. For labiomental wrinkle treatment and correction of the dimpled chin, please refer to these publications [1, 16, 17].

For a safe injection technique, it is essential to consider the vascular anatomy of this region. The submental artery and the facial artery as well as the accompanying veins are the main vessels in this region. The submental artery originates from the facial artery. It can anastomose with the mental artery, which arises from a branch of the maxillary artery. The submental artery can communicate with the inferior labial artery [18].

Posterior to the junction of the facial artery and vein from the neck over the mandible, the subcutaneous and supraperiosteal loge should be preferred for filler injections.

When selecting fillers, it is important to bear in mind that skin tightening effects are based on different effects. While hyaluronic acid (HA) fillers achieve a tightening effect primarily through volume, bioactive fillers such as poly-L-lactic acid and calcium hydroxyapatite (CaHA) are capable to change the connective tissue structure. However, this requires a comparatively longer time than the increase in volume using HA. The use of permanent fillers is not recommended, as severe side effects have been observed, sometimes with a delay of years. These usually result in surgical procedures to remove the filler material [19–23]. In the chin area, fillers

with a high G^* (gel strength or deformation resistance) and low $\text{Tan } \delta$ (phase angle, a relative measure of the viscous and elastic filler qualities) are recommended. $\text{Tan } \delta$ is the quotient of G'' (viscous modulus) and G' (elastic modulus).

The rheological properties of CaHA can be adjusted by appropriate dilutions. Higher dilutions reduce the gel strength (G^* and G'') and increase $\text{Tan } \delta$ and thus the viscosity [24].

FILLER STUDIES FOR CONTOURING THE LOWER JAWLINE

Table 1 provides information on study results after filler injection subcutaneously or supraperiosteally [25–34], both sharp and blunt needles were used. The injected volumes were between 1.2 and 4 ml. Most authors prefer a retrograde injection technique, some use the fanning or multilayered technique. Some of the authors treated only young patients, in whom aging processes in the lower third of the face are likely to be present only slightly, if at all [32]. Only one study focused on patients >50 years of age [33]. This highlights a general problem of studies in aesthetic medicine – the focus on youth and the exclusion of advanced age.



Fig. 2: Aesthetic filler treatment of the prejowl region with HA filler in a 65-year-old woman. Creation of the V-aspect in the frontal view by deep injection along the mandible anteriorly and correction of the mandibular fold with retrograde filler application. Above untreated, below immediately after injection.

Tab. 1: Studies on contouring the mandibular line.

| Studies | n | Filler | Outcome | Reference |
|---------|-----|---|---|----------------------------|
| RCT | 206 | Juvederm Volux vs. Untreated controls | FACE-Q Satisfaction after 6 months >70% "somewhat / very satisfied" | Burgess et al. 2024 |
| RCT | 175 | CaHA + lidocaine vs. untreated controls | Patient's Global Aesthetic Improvement Scale 94% "improved / very much improved" after 12 and 68.5% after 48 weeks; FACE-Q Satisfaction Score 73.3 (12 weeks) and 57.7 (48 weeks) | Green et al. 2024 |
| RCT | 98 | HA: Art Filler Volume vs. Juvederm Voluma | Clinician Global Aesthetic Improvement Score with 53% improvement after 18 months for both fillers | Braccini et al. 2023 |
| RCT | 10 | CaHA + Lidocaine in the half-face test | Clinician Global Aesthetic Improvement Score with an improvement of 2.3 points from 5 of Day 30-90 | Boen et al. 2022 |
| Retro | 41 | CaHA + Belotero Volume | Jawline Scale improves from 2.1 to 1.3 after 12 months | Fakih-Gomez & Kadouch 2022 |
| Open | 30 | Saypha Volume Plus Lidocaine | Clinician Global Aesthetic Improvement Score after 6 months 4.4, Patient Global Aesthetic Improvement Score 4.7; subjective patient-satisfaction after 12 months 4.5 | Müller et al. 2022 |
| RCT | 180 | CaHA + lidocaine vs. untreated controls | Response rate 76.5% (week 12), of which 67.3% also at week 48 | Moradi et al. 2021 |
| Retro | 30 | Juvederm Volux | Patient Global Aesthetic Improvement Scale "much improved" or "very much improved" at 96.7% after 20 days | Bertossie et al. 2021 |
| RCT | 20 | CaHA + and Micro-focused Ultrasound | Jawline Contour Score dropped from 2.2 to 1.9 after 15 months | Yutskovskaya et al 2020 |
| Open | 46 | CaHA + Lidocaine | Patient Global Assessment $\geq 9 / 94\%$, 6-8 / 6%, Physician Global Assessment $\geq 9 / 90\%$, 6-8 / 10%, after ≥ 12 months | Wollina & Goldman 2020 |
| RCT | 132 | Juvederm Volux vs. untreated controls | Clinician and Patient Global Aesthetic Improvement Score 100% / 91.8% after 3 months and 52.5% / 62.0% after 18 months | Ogilvie et al. 2020 |

Open – Open study; RCT – Randomized Controlled Trial; Retro – Retrospective study; CaHA – Calcium hydroxyapatite.

If the sagging cheeks are less pronounced, filler injections in the midface can also help to improve the lower jawline and should be performed first [35, 36].

Table 2 provides an overview of the fillers used.

FILLER FOR CONTOURING THE CHIN AND TREATING MENTAL WRINKLES

The injection point for the prejowl region is lateral to the paramedian retraction at the edge of the mandible. The filler is injected retrogradely submuscularly and/or subcutaneously (Fig. 2). The mental fold is often also treated by injecting hyaluronic acid fillers, which are injected subcutaneously [37].

The 3-point chin technique for shaping the chin goes back to Adel. All injection points are located along the

midline. The first injection point is at the mental crease. The second injection point is at the pogonion (the most anterior part of the chin) and the third injection point is at the menton (the inferior point of the chin). In a first step, a microbulus of hyaluronic acid filler is placed at these 3 points, followed by superficial retrograde linear injections [38].

Table 3 provides an overview of the filler studies [38–40].

FILLER FOR THE TREATMENT OF MARIONETTE LINES (MANDIBULAR FOLD)

In terms of the complex treatment of the lower third of the face, the mandibular folds should not be neglected. Hyaluronic acid fillers are predominantly used here, although case reports and retrospective studies

for CaHA are also available [32, 41–45]. Linear retrograde injection was predominantly used, with microdroplet or fanning techniques employed less frequently. The filler volume used was mostly 1ml.

SAFETY ASPECTS

In a systematic review, Ou et al. (2024) evaluated 917 patients with chin treatment. The most common side effects were at the injection site: swelling, bruising, pain, redness, pruritus. Only 2 more serious hub effects were observed, but no vascular complications (46). Other authors have observed tongue necrosis as a rare and serious complication [47].

SUMMARY

Filler injections have been established as non-surgical versatile tools to correct age-related changes in the aesthetics of the lower third of the face. Bio-stimulatory fillers such as CaHA are used for the jawline while hyaluronic acid fillers are preferred for the chin. However, permanent fillers should not be used due to safety concerns [22, 23]. There are some possible combinations with microfocused ultrasound, injection lipolysis and neuromodulators, which allow an individualized treatment [48]. There are also other treatment options such as lipotransfer and surgical techniques [49, 50].

The advantage of minimally invasive correction with fillers are the short downtime for the patient and the manageable costs. The disadvantage is the limited

duration of the effect. However, surgical measures cannot be replaced by fillers in cases of pronounced cheek ptosis and chin deformities.

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Tab. 2: Fillers used.

| Product name | Supplier | Remarks |
|--------------------|---------------------|---|
| Art Filler Volume | Fillmed | Tri-Hyal technology, 25 mg/ml HA, for the correction of deep volume losses |
| Art Filler Lips | Fillmed | Tri-Hyal technology, 25 mg/ml HA, for lip correction |
| Belotero Basic | Merz Aesthetics | CPM technology, 22.5 mg/ml HA, medium viscosity, monophasic |
| Belotero Volume | Merz Aesthetics | CPM technology, 26 mg/ml HA, highly viscous, good modellable, monophasic |
| Juvederm Volux | Allergan Aesthetics | Vycross technology, 25 mg/ml HA, very high cohesiveness, lifting force & elasticity |
| Juvederm Voluma | Allergan Aesthetics | Vycross technology, 20 mg/ml HA, high cohesiveness, lifting force & elasticity |
| Radiesse | Merz Aesthetics | Calcium hydroxylapatite microspheres in a Carboxymethylcellulose gel matrix, high elasticity and viscosity, long-lasting effect |
| Restylane Shaype | Galderma | NASHA HD technology, 25 mg/ml HA, high viscosity & elasticity, specially approved for the chin |
| Restylane Define | Galderma | Balance Technology, 20 mg/ml HA, high lifting capacity, biphasic |
| Revanesse Versa | Prollenium Medical | XpressHAN Technology, 20 mg/ml HA |
| Princess Volume | Croma-Pharma | BDDE-crosslinked HA, 23 mg/ml HA, monophasic |
| Saphya Volume Plus | Croma-Pharma | Cross-linked HA, 25 mg/ml, assumed residence time 12 months, monophasic |

HA – hyaluronic acid.

Tab. 3: Studien zur Behandlung des Kinns mit Fillern.

| Studies | n | Filler | Outcome | Reference |
|---------|-----|--|---|---------------------------|
| Open | 40 | Revanesse Versa | 5-Point Patient Satisfaction Score after 4 months 100% "extremely satisfied", after 6 months 87.5% | Adel 2024 |
| RCT | 140 | Resylane Shaype | Clinicians Global Aesthetic Improvement Scale 97% improvement after 3–12 months, Patient Global Aesthetic Improvement Scale 89% (3–12 months) | Nikolis et al. 2024 |
| RCT | 148 | Restylane Defyne | Chin Retrusion responder rates 84% and 61% (after 3 or 12 months), Clinician Global Aesthetic Improvement Score 97% and Patient Clinician Global Aesthetic Improvement Score 80% after 12 months | Xie et al. 2024 |
| RCT | 98 | Art Filler Volume vs. Juvederm Voluma | Clinician Global Aesthetic Improvement Score with 73% improvement after 36 Months for both fillers | Braccini et al. 2023 |
| Retro | 30 | Juvederm Volux | Patient Global Aesthetic Improvement Scale "much improved" or "very much improved" at 96,7% after 20 days | Bertossie et al. 2021 |
| Open | 46 | Belotero Basic or Princess | Patient Global Assessment $\geq 9 / 94\%$, 6–8 / 6%, Physician Global Assessment $\geq 9 / 90\%$, 6–8 / 10%, after ≥ 12 months | Wollina & Goldman 2020 |

Open – Open Study; RCT – Randomized Controlled Trial; Retro – Retrospective Study; CaHA – Calcium hydroxylapatite

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Tab. 4: Studien zur Behandlung der Mandibularfalten mit Fillern.

| Studies | n | Filler | Outcome | Reference |
|---------|-----|-------------------------------------|---|----------------------------|
| RCT | 100 | Art Filler Lips | Global Aesthetic Score after 3 week improvement at 94,4 %; after 18 Months at 33 % (injectors), 56 % (patients) | Ehlinger-David et al. 2023 |
| RCT | 20 | CaHA + and Micro-focused Ultrasound | Marionette Lines Score of 2.47±0.8 dropped to 1.8±0.7 after 15 months | Yutskovskaya et al. 2020 |
| Retro | 40 | CaHA (Wiederholung nach 12 Monaten) | Global Aesthetic Improvement Scale 2.7±0.7 (patients), 2.6±0.6 (doctors) after 12 months and 2.4±0.8 or 2.5±0.7 after 3–5 years | Wollina & Goldman 2020 |
| Open | 30 | Restylane Refyne / Restylane Defyne | Evaluation of “natural” mimik (2D-Video) “improved” by 80 % on day 42; Wrinkle Assessment Scale –2,15 (day 42); Global Aesthetic Improvement Scale “improved” or “very much improved” at 93,3 % at day 42 | Solish et al. 2019 |
| Open | 20 | Restylane /Perlane* | Investor & Patient Global Aesthetic Improvement Scale improved by 100% after 4 weeks; Wrinkle Severity Rating Scale improved | Brandt et al. 2011 |

Open – Open Study; RCT – Randomized Controlled Trial; Retro – Retrospective Study; CaHA – Calcium-Hydroxylapatite. *) Restylane Lyft.

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The FLYING WING EXCISION – the direct browlift for men

FRANK MUGGENTHALER

KEY WORDS: direct browlift, subcutaneous brow lift, browlift for males

SUMMARY:

Drooping eyebrows, whether due to age or congenital factors, can make a face look rather tired or simulate excess eyelid skin. An eyelid correction would be the wrong approach in these cases and could even cause a deterioration. A brow lift, on the other hand, is a very good way of adjusting the desired brow position, making the entire facial expression appear more alert and fresh. There are several brow lift methods to choose from, which differ in the choice of incision lines and preparation levels. Various methods that are generally quite suitable for women are not practical for men. The high or absent hairline on the forehead and the thicker forehead skin make it difficult to perform subcutaneous, subgaleal or subperiosteal brow lifts. In contrast, the eyebrows of men can be lifted very well and relatively easily after excision of a skin spindle directly above the brows. To achieve truly natural-looking results and to avoid aesthetically displeasing scars, it is necessary to choose a well-defined excision that is not crescent-shaped but rather trapezoidal or wing-like in outline and to apply a careful approach to wound closure and scar management.

INTRODUCTION

An open, friendly look and large, alert eyes are the main goals of all surgical procedures that are intended to give the face a younger and more harmonious expression. That is why eyelid correction is of particular importance in aesthetic facial surgery. It seems especially important to us to base the indication for an intervention on systematic considerations and to take into account possible combinations with other measures.

INDICATIONS AND TREATMENT CONCEPT

With advancing age, the forehead sags, causing the eyebrows to drop and creating the appearance of excess

eyelid skin, a condition known as pseudoblepharochalasis. This effect is particularly noticeable at the sides. As a result, the eye area appears smaller and loses its expressiveness, giving the face a tired and gloomy appearance overall.

This can be partially compensated for by increased activation of the frontalis muscle, but this leads to an increase in the formation of horizontal wrinkles on the forehead. Since the muscle mainly lifts the central area of the forehead, the position of the eyebrows changes, causing them to sink, especially at the sides. The apparent excess skin remains.

A well-defined eyelid crease and eyebrows that are positioned at least at the bony orbital margin or slightly above it are crucial for an open gaze and a youthful appearance. The shape and alignment of the eyebrows and a well-proportioned forehead height also contribute significantly to an overall harmonious appearance [1,2,3].

In the past, various techniques have been developed to raise the eyebrows, which can be used both in isolation and in combination with upper eyelid blepharoplasty. These techniques differ considerably depending on the dissection layer chosen, as well as the location and length of the incisions.

Each technique has its own advantages and disadvantages, which need to be carefully weighed against each other. Personally, I favour a limited subcutaneous brow lift because it is effective, relatively easy to perform, and adaptable to individual needs. We have had very positive experiences with this method in our clinic and mostly combine upper blepharoplasty with limited subcutaneous brow repositioning [4]. In many cases, excellent results can even be achieved by simply lifting the eyebrows. The apparent excess of eyelid skin then disappears completely as a result of raising the eyebrows.

DIRECT EXCISION IN MEN

In male patients in whom the hairline is far removed from the eyebrows or is completely absent, a subcutaneous brow lift may not be indicated because

excessive subcutaneous release of the forehead skin can endanger blood circulation. Scars cannot be hidden without hair present. A subcutaneous brow lift could theoretically be performed from a transverse forehead wrinkle, but this will always result in a visible scar, which can be cosmetically bothersome.

A suitable method for raising the eyebrows of men with a high or receding hairline is the direct excision of a skin spindle above the eyebrows [4,5]. This technique can achieve particularly effective and satisfactory results with thick and broad eyebrows. Careful selection of the incision and precise execution of the wound closure are necessary to leave scars that are as inconspicuous as possible.

The so-called 'direct excision' is a procedure that has been known for many years. Compared to other surgical techniques, it requires relatively little surgical effort and probably carries the least risk of recurrence. Nevertheless, this technique is rarely used. There are probably two main reasons for this:

The aesthetic result of the procedure often does not meet expectations. Noticeable scars may develop. However, in recent years we have found ways to develop solutions for both problems.

OUR APPROACH

To achieve aesthetically pleasing results, it is crucial to restore the eyebrows to the position they were in when the patient was younger. The descent of the eyebrows is due to the loss of skin elasticity, the action of gravity and the activity of two essential muscles, the frontalis muscle and the orbicularis muscle. The frontalis muscle has no bony insertion but is inserted in the subcutaneous tissue in the area of the eyebrows and is connected to the mobile galea aponeurotica, which extends over the head to the back of the head. This muscle lifts the eyebrows, which is important for both facial expression and opening up the field of vision. The muscle runs laterally along the temporal crest, which means that the outer parts of the eyebrows cannot be lifted even when the muscle is activated.

The orbicularis muscle runs like a ring directly below the eyebrows and laterally to the eye socket, just under the skin. Its function is to tighten the soft tissue around the eye socket. When the muscle is activated, the eyebrows are pulled down at the sides, creating the characteristic 'laugh lines' or 'crow's feet'. Both muscles, together with the loss of elasticity of the forehead skin, ultimately cause the eyebrows to descend more on the sides than in the middle area, with some descent towards the glabella as well. This causes the eyebrows to descend overall, but especially in the lateral third or quarter.



Fig. 1: Slices: divided, 1 to 7 cm long.

Dissection: subcutaneously, up to the orbital margin, or slightly caudal to it.

Fixation: temporarily with HEMOSTATIC NET sutures.

Anaesthesia: LA or analogous sedation. In combination with or as a replacement for an upper eyelid plastic surgery.



Fig. 2: Female patient before and six months after a limited subcutaneous brow lift and blepharoplasty of the upper lids.

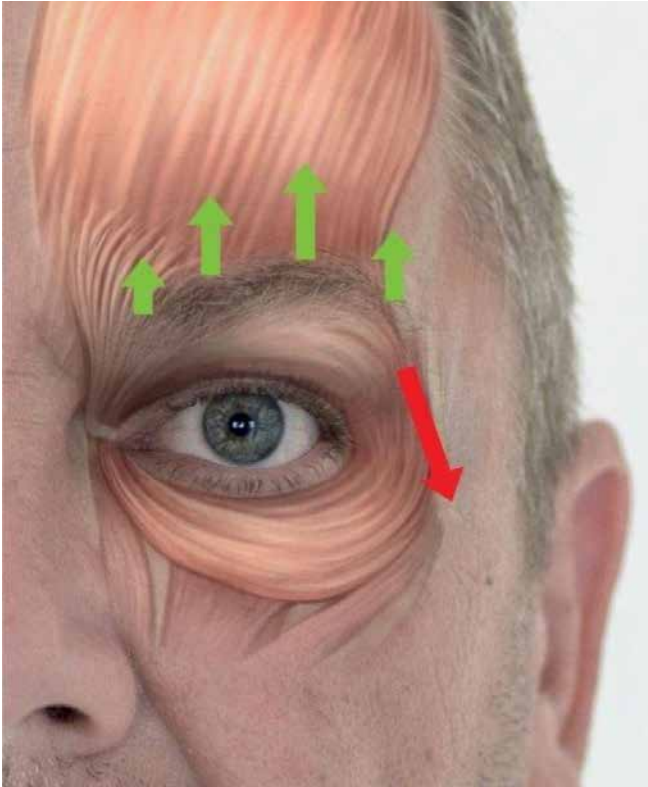


Fig. 3: To ensure an effective and harmonious eyebrow lift, these displacements of the eyebrows must be taken into account individually at each point.

THE FLYING WING EXCISION

The incision chosen by many surgeons, however, does not sufficiently take these requirements into account. If only a crescent-shaped area is chosen for the excision, the medial and especially the lateral end of the eyebrows are not raised (Fig. 4). Some authors even recommend excisions

that do not reach to the ends of the eyebrows [7]. This leads to only the medial part of the eyebrow being raised. Although this does open up the eye directly below it to some extent, the eyebrow takes on an unnatural concave shape.

Instead, we recommend determining the area of the excised tissue precisely according to the vectors along which all areas of the eyebrow have sunk downwards (Fig. 5). This results in a significantly larger excised area that extends medially beyond the end of the eyebrow into the area of the glabella and extends laterally more or less far into the temporal region. However, it is very important to allow the lower excision limits to rise slightly in order to avoid a downward-facing scar line after the wound edges have been approximated. Instead, a horizontal or even slightly ascending line should be created, whereby the lifting effect runs parallel to the vertically aligned vectors of descent. This leads to much more natural-looking results. The shape of the excised tissue is by no means similar to a crescent, but rather to a trapezoid or a wing that seems to hover directly above the eyebrow, thus creating a FLYING WING.

If the operation is carried out in this way, scars will inevitably develop that are not directly adjacent to the eyebrows. Since conspicuous scars can already develop when using a crescent-shaped incision, it is all the more important to use suitable techniques of wound closure and postoperative treatment when leaving the direct border to the hairy brow. This ensures optimal wound healing and the avoidance of conspicuous scars.

Some authors have recommended placing the incision at the upper edge of the eyebrows in such a way that the hair shafts are cut as tangentially as possible (8). This is said to cause the hairs to grow out of the follicles directly through the scars, concealing them. We recommend this procedure at the forehead-hairline border. However, we only rarely find this practical for the eyebrows, as the hairs often emerge from the skin at an

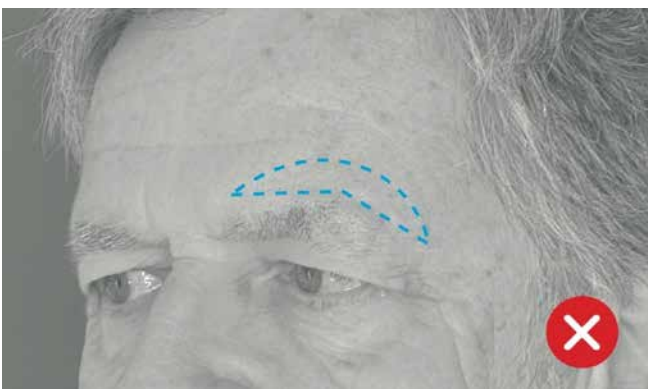


Fig. 4: If only a crescent-shaped area is chosen for the excision, the medial and especially the lateral end of the eyebrows will not be lifted.

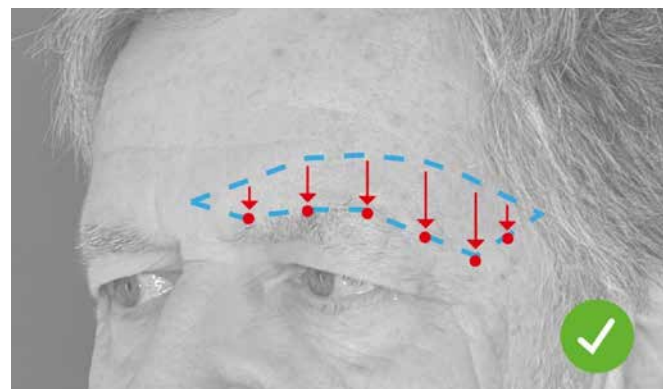


Fig. 5: We recommend determining the area of the excised tissue exactly according to the vectors along which all areas of the eyebrows have sunk downwards.

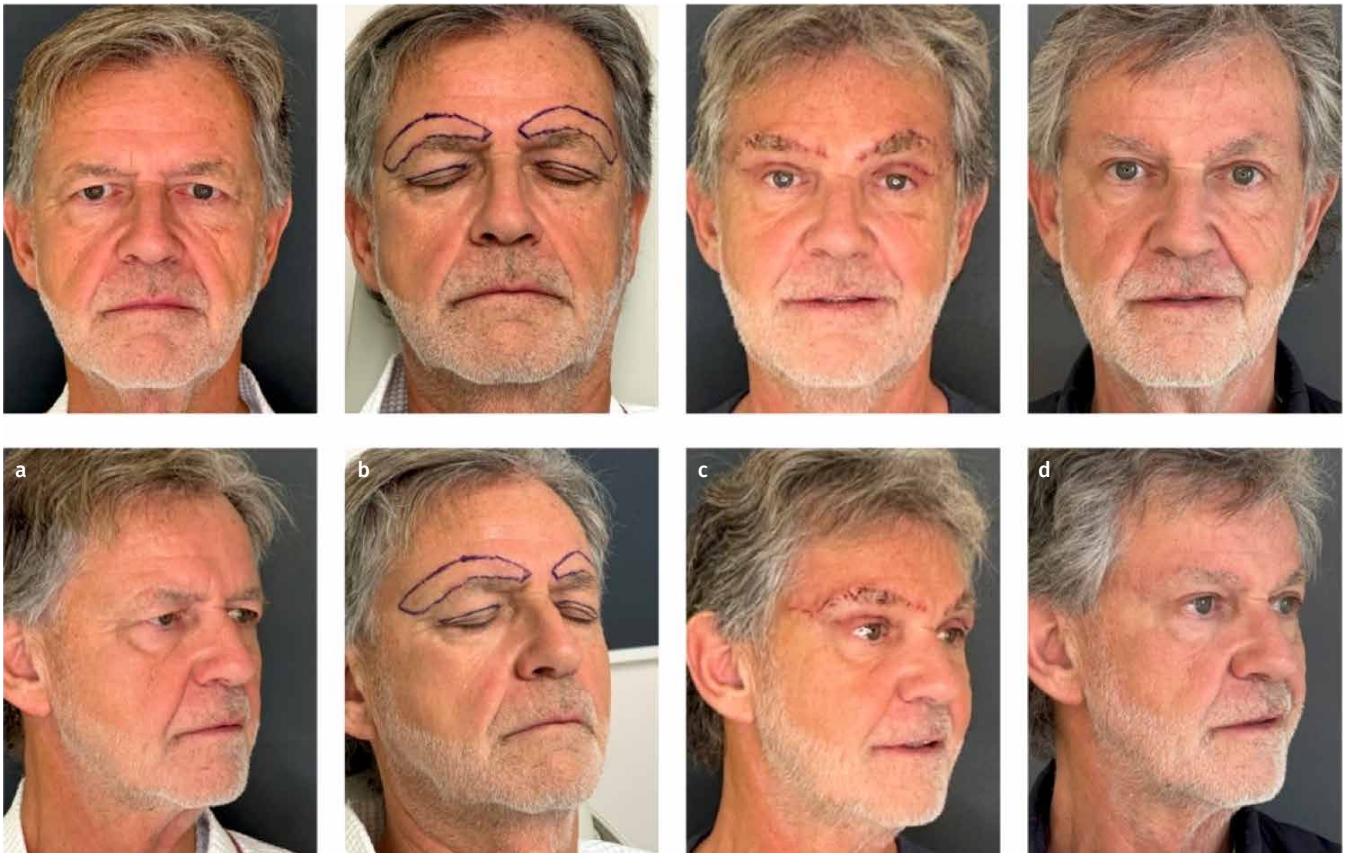


Fig. 6: Before (a), markings (b), 8 days after surgery (c) and 4 months after surgery (d).

oblique angle. This would require an extremely flat plane of incision, which in turn can lead to noticeable tissue bulging. This method is not possible anywhere other than on the eyebrows.

Instead, we recommend a multi-layer wound closure, which should be carried out on the surface with absolutely no tension, accompanied by an initial lifting of the suture line to compensate for the lowering of the scar that often occurs during the healing process. The subsequent treatment of the scars is particularly important. Here, we rely on a combination of different measures that have proven to be very effective in the

treatment of scars and hypertrophic scars in general. This consists of treatment with effective scar ointments several times a day, in particular KELI-MEDÒ ointment (Permamed), the application of IPL in two to four-week intervals and the treatment of scars with an erbium glass laser, also in two to four-week intervals. If there is thickening of the scar, 2 to 5 mg of triamcinolone injections can also be given per side at four- to six-week intervals.

Thanks to this combination treatment, we have so far been able to heal all scars so optimally that they were hardly visible later. Even in patients with barely formed

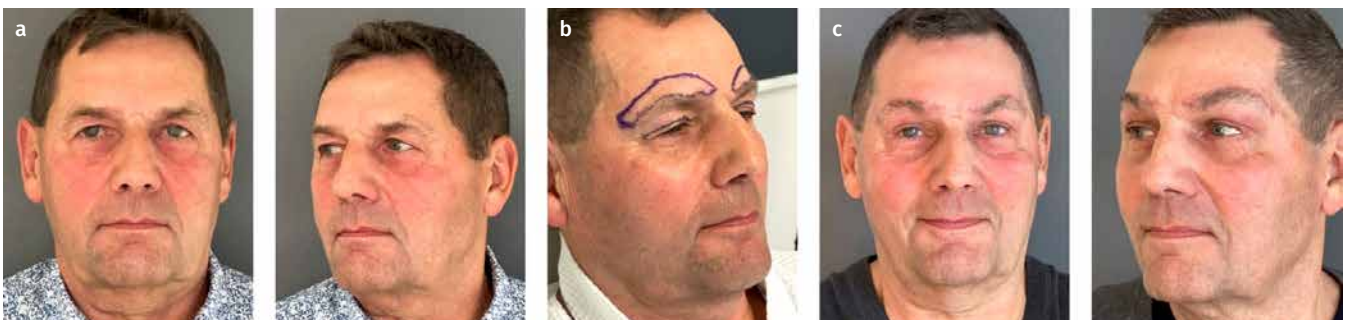


Fig. 7: Before (a), markings (b) and 2 months after surgery (c).



Fig. 8: Before (a), markings (b), excision (c) and 6 months after surgery (d).

eyebrows, we were able to achieve very good aesthetic results in almost all cases.

CONCLUSION FOR PRACTICE

To achieve a harmonious and natural-looking rejuvenation of the eye area, eyelid corrections are often requested by patients. In many cases, however, an eyebrow lift is required. This measure alone is often sufficient, so that a correction of the upper eyelids is not necessary. For women, we recommend a subcutaneous brow lift, in which the skin above the eyebrows is loosened and lifted via limited incisions at the hairline. However, this procedure is less successful for men. Here we recommend a direct excision.

To achieve good results, the excision area must not be crescent-shaped, but must be spindle-shaped, similar to a wing, i.e. a FLYING WING, and should extend both medially and especially laterally beyond the borders of the eyebrows.

To ensure optimal healing of the scars, we recommend a combination of a tension-free and erect wound closure, the application of an effective scar ointment, the use of IPL and erbium glass lasers, and, if necessary, triamcinolone injections.

Conflict of interest:

The corresponding author states that there is no conflict of interest.

Figures:

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MY·FILLER



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The best of two worlds: Hybrid fillers in aesthetic medicine

UWE WOLLINA^{1,2}, BHUSHAN MADKE²

KEYWORDS: aesthetic medicine, filler, hyaluronic acid, calcium hydroxyapatite, hybrid filler

SUMMARY:

Fillers are among the most widely used tools in minimally invasive aesthetic medicine. The main focus is on facial rejuvenation, but they are also used on the neck, décolleté, upper arms and hands. Fillers based on hyaluronic acid and biostimulatory fillers such as poly-L-lactic acid or calcium hydroxyapatite are the preferred choice. Their sequential use has been discussed in the past to improve the aesthetic result. Hybrid fillers consisting of two or more components are a relatively new development. This overview is intended to provide information on this. Hybrid fillers based on hyaluronic acid (HA), HA-calcium hydroxyapatite hybrids, HA-poly(D), L-lactic acid, HA-chitosan and HA-hydroxyapatite-pullan hybrids are presented.

INTRODUCTION

Fillers play a prominent role in clinical practice in the correction of signs of ageing of the skin and subcutaneous tissue. Among the temporary fillers, those based on hyaluronic acid (HAF) are the most popular, whereas collagen was used more frequently in the past. HAFs typically consist of chemically cross-linked HA molecules with different molecular weights, different HA concentrations and different degrees of cross-linking. The resulting hydrogels are enzymatically more stable against hyaluronidase and have optimised rheological qualities compared to non-crosslinked HA [1,2]. HA fillers

are apparently able to stimulate stem cells of the subcutaneous adipose tissue, which may contribute to the duration of the volume build-up effect [3].

In addition, biostimulatory, semi-permanent fillers such as poly-L-lactic acid (PLLA) or calcium hydroxyapatite (CaHA) are available, whose duration of action exceeds that of pure HA fillers. CaHA is a bioceramic active ingredient with very good tissue compatibility. Radiesse® (Merz Pharmaceuticals GmbH, Frankfurt/M.) is a CaHA filler in which 20–45 µm round, smooth microspheres of CaHA are incorporated into a carboxymethyl cellulose gel. After implantation, a tissue reaction occurs with increased formation of collagen I and III, elastin and proteoglycans. CaHA does not trigger a chronic inflammatory reaction [4]. However, CaHA depots show a temporary reduction in volume as a result of the degradation of the cellulose matrix. This loss is compensated with a time delay by the formation of new connective tissue. In addition, tissue tightening occurs [5].

PLLA is a biocompatible, biodegradable synthetic polymer. PLLA microparticles lead to a subclinical inflammatory reaction in the body, which stimulates the formation of new collagen. PLLA is supplied as a lyophilised powder for volume build-up. The filler is reconstituted with sterile water or physiological saline solution. After an appropriate hydration time, an injectable suspension is obtained. The injection treatment should be carried out several times (usually 2 to 3 times) in order to achieve an optimal result.

Artefill® (Suneva Medical Inc., San Diego, CA, USA) consists of microparticles between 40 µm and 63 µm, carboxymethylcellulose and non-pyrogenic mannitol [6]. Sculptra® Aesthetics (Galderma, Dallas, TX, USA) consists of 10–200 µm PLLA microparticles of different morphologies. The phagocytic content (<20 µm) is 46.3% ± 11.3% [7]. Clinical results with PLLA fillers indicate that in up to 80% of patients the volume effect is still fully maintained after 24 months [8].

For optimal results, the sequential application of different fillers was propagated [9, 10]. Hybrid fillers are a new development in the filler sector. The dictionary defines the term hybrid as “composed of different things, of two different origins”. Hybrid fillers based on

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HA currently exist, which combine low and high molecular weight HA, as well as fillers based on HA and CaHA. New developments are on the horizon.

HYBRID FILLER MADE FROM LOW AND HIGH MOLECULAR WEIGHT HA

Hybrid complexes of low and high molecular weight hyaluronic acid (HA) promote adipogenic differentiation and proliferation of somatic stem cells of the subcutaneous adipose tissue more strongly than cross-linked HA or linear low or high molecular weight HA [11].

This principle is followed by the filler Profhilo® (IBSA Farmaceutici Italia srl, Italy), which consists of stable, hybrid and co-operative HA complexes (HyCoCos). The thermal NAHYCO® hybrid technology is used for this purpose. The HA content is 32mg/mL. High-molecular HA (1,100–1,400 kDa) and low-molecular HA (80–100 kDa) are each contained at 32 mg in 2 mL in a buffered sodium chloride solution. The filler is characterised by very good biocompatibility and low viscosity. The Profhilo Structura® filler has a higher HA concentration of 45mg/mL, half high molecular weight (1400±200 kDa) and half low molecular weight (100±20 kDa) HA. The enzymatic cleavage and the stability of the filler implants in the tissue (200 µl) were investigated in vitro and in the murine animal model. Profhilo® was detectable in the subcutaneous tissue over 10 weeks using high-resolution ultrasound, Profhilo Structura® up to week 27 [12].

Both fillers were analysed in vitro with regard to enzymatic resistance. For this purpose, 1g of the respective filler was mixed with 20 mL of a hyaluronidase solution (8U/mL in PBS) at 37°C in a stirrer. Bovine hyaluronidase (type I-S, Sigma-Aldrich) was used. Profhilo Structura® was completely cleaved within 3h [12]. This property is of particular relevance in the event of accidental intravascular injection. Here, the time to complete dissolution of the filler is critical to avoid permanent tissue damage [13].

An open prospective monocentric study included 64 women aged 30–60 years (mean 53 years). Two therapy sessions were carried out 4 weeks apart for facial rejuvenation. The follow-up lasted 16 weeks. The following methods were used to quantify the success of the treatment: Wrinkle Severity Rating Scale (WSRS) – a 5-point scale from 1 (no wrinkles) to 5 (very severe wrinkles); Facial Volume Loss Scale (FVLS), – a 5-point scale, and the Beagley and Gibson Scale (BGS), a 4-point scale to assess the evenness of the skin's microrelief.

Furthermore, objective measurement methods were used such as optical colourimetry (Chromameter CR-200 Minolta, Osaka, Japan), corneometry (Corneometer CM825, Courage-Khazaka, Cologne, Germany), skin hydrometry (MoistureMeterD, Delfin Technologies, Kuopio, Finland), torsionometry (Dermal Torque Meter, DiaStron Ltd, Andover, UK), profilometry of nasolabial folds

Table 1: Possible indications for Profhilo®.

| Possible indication | Remarks |
|------------------------------------|--|
| Cheek structure | several studies, small series |
| Mandibular contouring | several studies, small series |
| Forehead wrinkles | Case report, with abobotulinum toxin |
| Neck with wrinkles and skin laxity | Case report, with abobotulinum toxin |
| Perioral wrinkles | Case report, with cross-linked HA filler |
| Skin laxity on the upper arm | Case report |

and marionette lines (Primos Software) and 3D photo documentation (Vectra H1, Canfield, Parsippany, NJ, USA). Based on this, the facial volume was also analysed before treatment, at weeks 8 and 16.

The BGS improved by 12.9%, the FVLS decreased by 18.2% and the WSRS by 14.7% by week 16. Hydration and surface relief improved, wrinkle depth decreased and facial volume increased slightly.

Side effects were reported by 9 participants (14%). These concerned slight haemorrhages at the injection site or slight oedema, which disappeared between 3 and 10 days after injection [14].

Profhilo® Structura was used to build up the midface in a retrospective half-side study of 22 patients aged 36–60 years (mean 53 years). Two injections of 2 mL of the filler were administered. The follow-up period was 6 months. The filler showed pseudoplastic properties immediately after injection and was integrated into the subcutaneous fatty tissue. The volume increase was stable over 6 months. Patient satisfaction was high. No side effects were observed [15].

In a post-marketing study, >40,000 patients who had been treated with Profhilo® were analysed. In the years 2015–2018, 12 adverse reactions were reported worldwide. Early reactions at the injection site were swelling, oedema, erythema, ecchymosis. Local late reactions (<72h) involved swelling and nodules, which indicates a very good safety profile [16].

In an open study, 10 patients with skin laxity on the neck (≥type 3 according to the Glogau Wrinkle Scale; GAIS score) aged 35 to 65 were included. Two therapy sessions were carried out. In the first session, plasma ablation was combined with an HA injection. After 30 days, the second treatment was performed with HA alone. After a further 30 days, the success of the treatment was assessed. A GAIS score of 1 or 2 was found in 90% of cases (patient view and investigator). Pain during treatment was reported as a median of 2.4 out of 10 on the VAS scale. Minimal side effects such as erythema and oedema were only temporary. There were no serious

side effects [17]. Table 1 provides an overview of possible indications [18].

HYBRID FILLER MADE FROM HA AND CAHA

HARmonyCa® (Allergan Aesthetics, an AbbVie Company) is a hybrid filler containing hyaluronic acid HA (20 mg/mL) and calcium hydroxyapatite (CaHA; 55.7%; microspheres with a diameter of 25–45 µm) as well as 0.3% lidocaine in a 1.25-ml prefilled syringe.

In a monocentric, prospective split-face study, 14 female patients and one male patient aged between 32 and 63 years were treated for cheek ptosis. The Fitzpatrick skin phototype was between II and IV. The Physician Global Aesthetic Improvement Scale, the Subject Global Aesthetic Improvement Scale scores and a validated 5-point scale for the lower third of the face were used to quantify treatment success [19]. Patients with “mild sagging” and “moderate sagging” were included.

The injection was made via two points in a retrograde linear fan style. The first injection was placed subzygomatically 5 cm below the lateral orbital rim, the second above the mandible on the anterior edge of the masseter muscle. One prefilled syringe of 1.25 ml was used on each side of the face. The patients were followed up for 120 days. Photo documentation was carried out using the Vectra 3D Imaging System from Canfield.

At the end of the follow-up period, all participants showed an improvement in the Physician Global Aesthetic Improvement Scale, 40% of whom had above-average scores. The Subject Global Aesthetic Improvement Scale scores were very significantly improved in 14 of 15 patients, 1x significantly improved. The skin thickness had increased on average from 1.47 ± 0.08 mm to 1.68 ± 0.08 mm after 120 days. Tolerance was very good. Pain, mild oedema and ecchymosis were observed in some cases during and immediately after injection. One patient developed a small papule on the lower half of the face. There were no serious side effects [20].

A prospective intervention study on facial rejuvenation with 15 patients used the hybrid filler in the preauricular region. 1.25 ml per side was injected retrogradely. The participants underwent a sonographic examination, elastography and photographs using 2D and 3D techniques. Follow-up was performed for 180 days after treatment.

The median volume had increased by 2.1 cm per side³. The tension vectors increased by 2.2 mm and 2.0 mm respectively. The elastography measurements indicated an increase in collagen fibres from day 60 onwards. Minor redness and inflammation were observed as side effects, which disappeared again within 48 hours. Severe side effects did not occur [21].

In a retrospective study, 243 patients who had received at least one treatment with HARmonyCa® and were followed up for at least 12 months (median 15.4 months) were analysed: Of these, 94.0% were women

with a median age of 50.1 years. The predominant Fitzpatrick skin phototypes were II and III with 80.1%. An average of 2.2 mL (0.5–8.9 mL) of filler was injected per treatment session. The cheeks (71.2%) and the mandibular region (69.7%) were favoured for treatment. 11 patients (12 treatments) experienced adverse events as a result of the hybrid filler, most of which were mild. Specifically, these were tissue hardening (3, 0.7%), oedema (3, 0.7%) and non-inflammatory lump formation at the injection site (5, 1.2%). In the long-term follow-up, there were 15 (6.2%) patients with 16 documented adverse reactions (6x oedema, 5x injection site nodules, 1x inflammation, 3x skin induration, 1x hypersensitivity reaction). No serious side effects were observed [22]. Table 2 provides information on possible indications [20–25].

The combination of (CaHA) and (HAF) filler in one cannula represents a hybrid filler. Radiesse® and Belotero® (Merz Pharmaceuticals GmbH, Frankfurt/M.) were used in 2112 patients with this concept. The follow-up was at least 12 months. Various mixing ratios were used. Only 5 minor side effects (0.24%) were registered. These were non-inflammatory nodules (n=4) and one transient oedema. Two of the nodules disappeared completely after hyaluronidase injection [26].

In a prospective monocentric study, 25 patients were included who achieved a score of 1–2 on the Merz 5-point scale for the nasolabial fold and mandibular contour. A mixture of 1 mL HAF, 0.5 mL lidocaine and 1.5 mL CaHA was used. A total of 3 mL of filler was injected. The results were recorded using the visual analogue scale (VAS) and the 5-point Global Satisfaction Scale (GSS) from the examiner's and patient's perspective. In some of the patients, an additional 0.1 mL of CaHA or the CaHA/HAF mixture was injected retroauricularly and removed after 6 months for histological examination. The median VAS and GSS scores improved. Histological examination showed increased collagen without inflammation. Patient satisfaction was high. The CaHA/HAF mixture compensated for the temporary early volume loss of the CaHA filler [27].

A retrospective evaluation of CaH/HAF therapy for the middle and lower third of the face utilised the Merz Aesthetics Scale for the Jawline® (MAS). Forty-one

Table 2: Possible indications HARmonyCa®

| Possible indication | Remarks | Reference |
|---|-------------------------------------|-----------|
| Cheek augmentation | prospective & retrospective studies | [20–24] |
| Contouring of the lower third of the face | prospective & retrospective studies | [20, 23] |
| Sunken acne scars | Case report | [25] |

patients were included. The median age was 47.5 years (21–63 years). The median MASJ score improved from 2.12 before therapy to 0.68 after 3 months and 1.27 after 12 months. All participants experienced a ≥ 1 score point improvement after 3 months compared to 85% after 12 months. No undesirable side effects were observed [28]. The combination with botulinum toxin A (incobotulinum toxin A; Xeomin®; Merz) in a syringe is known as „The gold protocol“ and has been propagated for the rejuvenation of the soft tissues of the neck [29].

In a double-blind prospective study, CaH/HAF was used in a 1:1 ratio with CaH alone for rejuvenation of the back of the hand. The results were assessed using the Global Aesthetic Improvement Scale (GAIS) and the Manchester Hand Grading System (MHGS) and objectively recorded using cutometry, corneometry and ultrasound. GAIS and MHGS did not differ significantly in both groups. Hydration, skin elasticity and skin thickness improved in both treatment arms. Higher echogenicity was found in the hybrid arm, which was interpreted as increased tissue biostimulation. No side effects were observed, so that the methods were classified as safe [30].

Stimulate® (MatexLab SA, Lugano, Switzerland) contains 26mg/mL HA, 1% CaHA and the amino acids L-proline and glycine. Polyethylene glycol serves as the cross-linking molecule, which is why it is also referred to as pegylated HA. Stimulate® One has 28mg/mL HA. The average half-life of the filler after implantation is given as 6 months.

In vitro studies showed no evidence of cytotoxicity (HaCaT keratinocytes), changes in cell morphology and viability and intracellular F-actin microfilaments [31]. The filler stimulates collagen production in vitro in fibroblast culture and in vivo in human skin [32, 33]. The filler has an anti-inflammatory effect on neutrophil granulocytes [34].

In a prospective, monocentric real-life study, 70 patients were included, 60 of whom completed the study after 6 months. The median age was 59 years (range: 26–70 years). The filler was injected once with a maximum of 1mL per side to fill volume deficits in the cheek region. The following measurements were taken: The 6-point Mid-Face Volume Deficit Scale (MFVDS), the Global Aesthetic Improvement Scale (GAIS) and the Patient Satisfaction Score (PSS) on a 10-point VAS scale. Over 80% of the patients achieved 3 score points in the MFVDS before the start of treatment, the remaining patients had a higher volume average. Immediately before and after treatment, the MFVDS averaged 3.20 and 1.77. After 3 and 6 months, the values were 1.40 and 2.62. The GAIS averaged 2.27 before treatment and improved to 1.72 and 1.95 in months 1 and 2. The VAS values for patients and investors were in the same range between 93% (3 months) and 100% (immediately after injection). They fell to around 70% at month 6. No severe side effects were observed [35].

Table 3: Possible indications for hybrid fillers made from Radiesse® and Belotero®

| Possible indication | Remarks | Reference |
|----------------------------|----------------------------------|-----------|
| Nasolabial fold | uncontrolled study | [27] |
| Contouring of the mandible | retrospective study | [28] |
| Neck rejuvenation | Case report, additionally BoNTA* | [29] |
| Hand rejuvenation | double-blind study | [30] |

*BoNTA – Botulinum toxin type A.

Table 3 provides an overview of possible indications.

POLY-L-LACTIC ACID AND HYALURONIC ACID

Poly-L-lactic acid (PLLA) is a biostimulatory filler and is considered the first long-acting collagen stimulator [36].

A hybrid filler consisting of HA, PLLA and polynucleotides (PN) was presented by Oh et al. (2021). PN is considered a growth factor for fibroblasts and osteoblasts. The PLLA microspheres in this filler are smaller and rounder than in the classic PLLA fillers. HA-PN/PLLA has a higher viscosity and elasticity (G') with comparable osmolality to HA and PN fillers. In animal experiments, this new filler showed persistence in the tissue for 24 weeks [37].

The filler Reversal® PLA+HA (Koru Pharma; Seoul, South Korea) contains 30mg HA and 170mg poly-D, L-lactic acid per 200mg vial. The viscosity is stated as 44.6Dl/g. Juvelook® and Juvelook® Volume are also HA hybrid fillers with poly-D, L-lactic acid (LV Plastic Surgery, Seoul, South Korea). Juvelook® Volume contains 170mg of polylactic acid microparticles with a diameter of 50µm to 60µm and 30mg of non-crosslinked HA. AestheFill® (Regen Bio Global Inc., Seoul, South Korea) – a hybrid filler of poly-L, D-lactic acid and HA was tested in a multicentre controlled study against HA in the correction of nasolabial folds. A total of 260 patients were included. After a single injection, follow-up was carried out over 52 weeks. The authors used the Wrinkle Severity Rating Scale (WSRS) and the Global Aesthetic Improvement Scale (GAIS) to quantify the treatment results.

At week 24, 67.6% of patients in the AestheFill® group and 60.9% in the HA group showed an improvement in WSRS of at least one degree. The hybrid filler was superior to the HA filler at all time points. There were no serious side effects [33]. For possible indications, see Table 4, where different dilutions of the lyophilisate are used [38, 39].

Table 4: Possible indications for hybrid fillers made from poly-D, L-lactic acid and hyaluronic acid

| Possible indication | Dilution |
|--|----------|
| Chin or nose augmentation | 1,5–3 x |
| Deep facial wrinkles (nasolabial, mentolabial) | 3–6 x |
| Flat facial wrinkles, lower eyelid | 6–12 x |
| Skin booster | 12–24 x |

PLLA in an HA suspension (PLLA-b-PEG) utilised round, smooth PLLA microspheres (diameter 20–45 µm). In animal experiments, the volume increased in the first 4 weeks after implantation of the filler and then gradually decreased. Fibrous tissue, vascular density and collagen fibre formation increased over 26 weeks after injection. Studies of patients seeking facial contouring showed significant improvements in the Global Aesthetic Improvement Scale 3 and 12 months after injection. Even after 12 months, 90% of patients still showed good contouring with minimal side effects [40, 41].

NEW HYBRID FILLERS

A hybrid hydrogel of HA and pullulan was analysed in vitro. Pullulan is a natural, water-soluble linear polysaccharide consisting of maltotriose units. Biomimetic hydroxyapatite spheres were incorporated into this gel. Silane couplers were used to improve the physicochemical, mechanical and biological properties. This hybrid gel was tested in body fluids. The hydroxyapatite spheres showed a uniform distribution in the gel. The elastic modulus G' , viscosity, resistance and stability could be improved by the spheres. The gel showed a high resistance to enzymatic biodegradation. In cell cultures with L-929 fibroblasts, their adhesion and distribution improved, especially on the spheres. Cell viability was increased [42].

Another new approach is the use of lactose-modified chitosan (CTL; CHITLAC®) to save crosslinker molecules – HA-CTL filler. CTL can be enzymatically degraded completely by lysozyme and partially by hyaluronidase. HA was crosslinked with different amounts of 1,4-butanediol diglycidyl ether (BDDE) (degree of modification 3.5–8.8%) and CTL was added: 20–25 mg/mL and 5 mg/mL for HA and CTL, respectively. Due to its anionic nature, CTL is able to interact with the cationic HA. This increases the elastic modulus G' . The loss factor $\tan \delta$ (quotient of G''/G') decreases. This type of filler appears to be more resistant to shear forces and pressure. By varying the HA modification (MoD%) with BDDE, higher-molecular HA and increasing the HA concentration from 20 to 25 mg/mL, the elasticity performance could be increased to 94%. For the practical use of the filler, however, it must

also be noted that it must remain injectable. Therefore, a product with a slightly lower MoD% is preferable for clinical use. Cohesiveness, hydrolysis resistance and swelling of HA-CTL were comparable with commercial HA fillers. The HA-CTL filler with the lowest degree of cross-linking showed a swelling of 89%, which was significantly lower than that of commercial fillers (100–300). This enables more precise work, e.g. on the lips.

HA-CTL fillers can be adapted to specific requirements depending on the indication by changing the degree of cross-linking in the viscosity and cohesiveness. In the in vitro tests, this filler group showed significantly higher values of the normal force FN under static pressure than commercial HA fillers, which indicates very good lifting properties [43].

SUMMARY AND OUTLOOK

Hybrid fillers expand the armamentarium of minimally invasive options for aesthetic medicine. Rheological properties, biostimulatory effects and safety profiles can be optimised in this way. At the same time, possible disadvantages of existing filler products are overcome or reduced. The application possibilities are extended. The safety profile is very good.

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FILLERS FOR SUPERFICIAL AUGMENTATION

| Product name | Company | Indications | Application depth | Material i.e. hyaluronic acid concentration and crosslinkage | Needle and/or cannula size | Special material properties |
|--|---|---|-------------------------------------|--|---|--|
| ART FILLER® FINE LINES 2x1ml | FILLMED Laboratoires | SOFT & SMOOTHING: For fine and superficial wrinkles and lines, also periorbital as well as perioral | Upper dermis | 20 mg/ml cross-linked hyaluronic acid plus 0.3% lidocaine. | Needle: 4 x 30 G | TRI-HYAL® technology for natural results: Network of very long as well as long HA chains and free hyaluronic acid + optimized BDDE concentration |
| BELOTERO® Soft | Merz Aesthetics | Fine line correction such as perioral lines | Superficial to mid dermis | 20 mg/mL dynamically multi-crosslinked HA (CPM®-Technology) | Needle: 30 G 1/2 | Polydensified, cohesive gel, very good tissue integration, low water binding. Blanching possible, available with lidocaine (0.3%) and without lidocaine |
| Estyme® SMOOTH | Manufactured by Symatase; Distributed by Evolus, Inc | Indicated to correct nasolabial folds and perioral lines. | Injected into dermis to hypodermis. | 20 mg/ml cross-linked hyaluronic acid plus 0.3% lidocaine | 30G Needle (provided) 25G Cannula (not Provided) | Estyme is a next generation injectable hyaluronic acid made using Cold-X™ Technology by Symatase. |
| HYABELL® Lips + Lidocaine | Adoderm GmbH | Definition of lip contours, and hydration of the lips | Lips: sub-dermal | 12 mg/ml cross-linked hyaluronic acid plus 0.3% lidocaine. | Needle: 27 G | Exceptionally soft injection: intermediate value of 10NatG and G* with 0.1Hz is lower than 35 Pa; for excellent properties in shaping and distribution of the filler; for natural and elegant appearance of lip volume, low water uptake |
| Hydro Deluxe | NEAUVIA® | Improvement of skin quality | Epidermis and dermis | Hyaluronic acid content: 18 mg/ml Amino acids & CaHA: Glycine, L-Proline & 0.01 % CaHa Crosslinker: Uncrosslinked HA | Needle: 4 x 30 G 1/2" | Contains 18 mg/ml of pure hyaluronic acid and is enriched with 0.01% calcium hydroxylapatite, glycine and L-proline. This unique composition creates the optimal environment for the physiological restoration of the skin |
| Hydro Deluxe Man | NEAUVIA® | Improvement of skin quality | Epidermis and dermis | Hyaluronic acid content: 18 mg/ml Amino acids & CaHA: Glycine, L-Proline & 0.01 % CaHa Crosslinker: Uncrosslinked HA | Needle: 4 x 30 G 1/2" | Contains 18 mg/ml of pure hyaluronic acid and is enriched with 0.01% calcium hydroxylapatite, glycine and L-proline. This unique composition creates the optimal environment for the physiological restoration of the skin |
| Intense Rheology | NEAUVIA® | Filling of wrinkles and fine lines | | Hyaluronic acid content: 22 mg/ml Amino acids: Glycine & L-Proline Crosslinker: PEG (polyethylene glycol) | Needle: 2 x 27 G 1/2" | Soft and lightweight PEG-HA filler that gives the gel a low stamp pressure, making it perfect for fine lines and wrinkles. The product can still be physiologically integrated and remains flexible so that no deformation occurs. Due to its thermostable properties through PEG cross-linking, can be combined with NEAUVIA Energy-Based-Devices. |
| Juvéderm® ULTRA 2 | Allergan Inc. | Filling of medium deep wrinkles, definition of the lips | Mid dermis | 24 mg/mL crosslinked HA (HYLACROSS-Technology™). | Needle: 30 G 1/2 | Smooth gel, well tolerated, long lasting, good durability up to 12 months, with lidocaine (0,3 %) |
| Juvéderm® VOLBELLA with Lidocaine | Allergan Inc. | Superficial and medium-deep wrinkles, definition of lip contours | Upper and mid dermis | 15 mg/ml cross-linked HA, unique, patented VYCROSS Technology™, with long and short chain HA acids - for particularly fast tissue integration, long duration and low swelling of the gel | Needle: 30 G 1/2 | Good duration, good dispersion (reason: low cohesion), with lidocaine (0.3%). Results visible for up to 12 months |

| Product name | Company | Indications | Application depth | Material i.e. hyaluronic acid concentration and crosslinkage | Needle and/or cannula size | Special material properties |
|---|---------------------------------|---|--|---|--|---|
| Juvéderm® HYDRATE | Allergan Inc. | Improvement of skin moisture and elasticity | Upper dermis | 13.5 mg/mL cross-linked HA with 0.9 % manitol | Needle: 30 G 1/6; 32 G | Good water absorption, low durability |
| Juvéderm VOLITE – Skin Juvénizer | Allergan Inc. | Improving skin quality factors moisture and elasticity. Smoothing fine wrinkles on the face, décolleté and hands | Intra dermal | 12 mg/ml cross-linked HA, unique, patented VYCROSS Technology™, with long- and short-chain HA acids - for particularly fast tissue integration, long shelf life and low swelling of the gel | Needle: 32G 1/2 | Only one application: results visible for up to 9 months. Significant hydration and patient satisfaction, contains lidocaine (0.3%) |
| PERFECTHA® Finelines | Sinclair Pharma | Superficial wrinkles and skin depressions, periorbital lines, perioral lines (i.e. fine smokers lines) | Superficial dermis | 20 mg/g hyaluronic acid (non-animal, mixture of 90% cross-linked and 10% non-cross-linked hyaluronic acid), cross-linking agent BDDE (<1%) | Needle: 30 G x 13 mm | E-Brid™-Technology; safe, well tolerated, easy to inject, high lifting and volumizing capacity, long lasting |
| PERFECTHA® Fine Lines Lidocaine | Sinclair Pharma | Superficial wrinkles and skin depressions, periorbital lines, perioral lines (i.e. fine smokers lines) | Superficial dermis | 20 mg/g hyaluronic acid (non-animal, mixture of 90% cross-linked and 10% non-cross-linked hyaluronic acid), cross-linking agent BDDE (<1%) | Needle: 30 G x 13 mm | E-Brid™-Technology; easy to inject, well tolerated, light lifting capacity |
| MaiLi Precise | Sinclair Pharma | Facial reconstruction for congenital or disease-related structural defects: Scar tissue Aesthetic treatment of fine lines or moderate skin deformities lip definition or augmentation periorbital area (tear trough) | Dermis; intra/sub-cutaneous or between mucosa and muscle | "15mg/ml HA concentration; 3mg/ml lidocaine" | Needles: 4 x 30G/ packing unit | OxiFree™ technology; very supple gel with strong projection force at the same time |
| My Filler Soft | My Med Aesthetics | Super hydration of periorbital (dark circles), perioral (smoker's wrinkles), natural-looking skin and hydrated lips | Upper dermis | 20 mg/ml monophasic cross-linked HA. TRIO technology | Needle: 27 G, 30G, 32 G | Low viscosity and powerful hydration |
| NCTF® 135HA 5x3ml" | FILLMED Laboratoires | For the treatment of fine wrinkles and radiance Especially also for face, neck, décolleté, back of the hand. | Epidermis, upper dermis | 5 mg/ml Hyaluronic Acid +. Active ingredient complex: 12 vitamins + 24 amino acids + 6 co-enzymes + 5 nucleic acids + 6 minerals + 6 other substances | Needle: 5 x 30 G (12 mm) 5 x 32 G (4 mm) | Innovative formulation with 59 active ingredients. Scientific expertise since 1978 |
| Restylane® Fynesse™ | Galderma | Superficial wrinkles (especially perioral and periorbital) | Superficial dermis | 20 mg/ml HA, gel with moderate crosslinkage and low calibration grade (Balance technology) | Needle: 30 G 1/2 (UTWN) Canula: Steriglide (TSK) 30 G | Very Soft gel with moderate lifting capacity |

| Product name | Company | Indications | Application depth | Material i.e. hyaluronic acid concentration and crosslinkage | Needle and/or cannula size | Special material properties |
|--|----------------------------|---|---|--|---|---|
| Revanesse® Pure™+ | Prollenium | Superficial and perioral lines and wrinkles. | Superficial dermis | 14 mg HA, 100% linear HA | 30 G | Next Generation HA Filler with proprietary Thixofix Technology and with Lidocaine. |
| Revanesse® Revise™+ | Prollenium | Superficial to moderate lines and wrinkles, volume restoration, lip augmentation, skin hydration and contouring of depressions | Superficial to mid dermis | 12 mg cross-linked HA gel | 30 G | Next Generation HA Filler with proprietary Thixofix Technology and with Lidocaine. |
| Revanesse® Kiss™+ | Prollenium | Lip augmentation, perioral lines, superficial lines and wrinkles | Superficial to mid dermis | 25 mg crosslinked HA gel, 10% linear HA | 27 G | Next Generation HA Filler with proprietary Thixofix Technology and with Lidocaine. |
| saypha® RICH | Croma Pharma | The product is a viscoelastic solution and compensates for the loss of hyaluronic acid due to the aging process, moisturizes the skin, improves the tone and elasticity of the skin and fills small wrinkles such as crow's feet, smile lines or smoker's lines around the mouth | Superficial dermal tissue, preferably deeper | 1.8% non-cross-linked, native HA (18 mg/mL) and 2.0% glycerol (20 mg/mL) | 2 x 30 G 1/2" thin wall Terumo™ needles (CE 0197) | Glycerin (a polyalcohol) is a natural component of the skin. In saypha® RICH it has a dual function: it protects the hyaluronic acid molecules from degradation and at the same time promotes skin hydration and elasticity. In extensive tests the high-quality glass syringes from significantly better E&L profile than any plastic syringe. |
| STYLAGE® S | Laboratoires VIVACY | Correction of first wrinkles and for filling of small and mid-deep wrinkles | Upper to mid dermis | 16 mg IPN cross-linked HA with added antioxidant mannitol | Needles: 4 x 30 G 1/2" | IPN crosslinked HA with double 3D-matrix and antioxidant for reduction of possible swelling and hematomas. |
| STYLAGE® S Lidocaine | Laboratoires VIVACY | Correction of first wrinkles and for filling of small and mid-deep wrinkles | Upper to mid dermis | 16 mg IPN cross-linked HA with added antioxidant mannitol & lidocaine (0.3%) | Needles: 4 x 30 G 1/2" | IPN crosslinked HA with double 3D-matrix and antioxidant for reduction of possible swelling and hematomas |
| STYLAGE® HYDROMAX | Laboratoires VIVACY | For mesotherapy and intensive hydration of the skin with long shelf life (4-6 months) | Mid dermis | 12.5 mg uncross-linked HA with added antioxidant sorbitol | Needle: 1 x 30 G 1/8" | Very high water binding capacity due to the antioxidant sorbitol |
| TEOSYAL PURESSENSE REDENSITY® 1 | TEOXANE | Beauty booster to prevent signs of aging, hydration and densification of the skin. Improvement of skin quality face, neck and décolleté | Superficial to mid dermis - only superficial dermis | Hyaluronic acid: non-crosslinked HMW-HA HA-concentration: 15 mg/ml | Needle: 30 G 1/2" | Proven effectiveness in moisturizing, restructuring and densifying the skin. Syringe volume: 2 x 1 ml or 1 x 3 ml Lidocaine: 0.3% Degree of modification: 0% |
| TEOSYAL RHA® 1 | TEOXANE | For the treatment of dynamic, superficial wrinkles on the face, neck and décolleté: In the perioral and periorbital areas, wrinkles of the forehead and neck, as well as to improvement of skin quality. Recommended in combination with REDENSITY® 1 for skin quality treatments (face, neck, décolleté) | Superficial to mid dermis | Hyaluronic acid: non-crosslinked HMW-HA HA-concentration: 15 mg/ml | Needle: 30 G 1/2" | Very sculptable gel with high elasticity for filling fine wrinkles on the face, neck and décolleté. Preserved Network Technology for natural-looking results and a duration of action of 12 months and longer. Syringe volume: 2 x 1 ml Lidocaine: 0.3% Degree of modification: ~ 1.9% |

FILLERS FOR MEDIUM DEEP AUGMENTATION

| Product name | Company | Indications | Application depth | Material i.e. hyaluronic acid concentration and crosslinkage | Needle and/or cannula size | Special material properties |
|---|---|---|-------------------------------------|---|---|--|
| ART FILLER® UNIVERSAL 2x1.2ml | FILLMED Laboratoires | FILL & SHAPE: For the treatment of medium to deeper wrinkles + lips. | Medium to deep dermis | 25 mg/ml cross-linked hyaluronic acid plus 0.3% lidocaine | Needle: 4 x 27 G | TRI-HYAL® technology for natural results: Network of very long as well as long HA chains and free hyaluronic acid + optimized BDDE concentration. |
| ART FILLER® LIPS SOFT 1 x 1ml | FILLMED Laboratoires | SHAPING & HARMONIZING: For the treatment of lip contour, perioral wrinkles as well as for subtle lip volume | Mucosa (+ medium deep dermis) | 25 mg/ml cross-linked hyaluronic acid plus 0.3% lidocaine | Needle: 2 x 30 G | TRI-HYAL® technology for natural results: Network of very long as well as long HA chains and free hyaluronic acid + optimized BDDE concentration |
| BELOTERO® Balance | Merz Aesthetics | Nasolabial folds, marionette lines, perioral folds, moderate oral commissures and lip augmentation | Superficial to mid dermis | 22.5 mg/mL dynamically multi-crosslinked HA (CPM®-Technology) | Needle: 27 G 1/2, 30 G 1/2 | Medium viscose poly-densified cohesive gel. Very good tissue integration, almost no water retention. Estimated duration: 12 months. Very well tolerated, blanching injection technique possible, available with lidocaine (0.3%) and without lidocaine. |
| BELOTERO® Intense | Merz Aesthetics | Correction of deeper lines, such as nasolabial fold and marionette folds; lip volume | Mid and deep dermis | 25.5 mg/mL dynamically multi-crosslinked HA (CPM®-Technology) | Needle: 27 G 1/2 | High viscose polydensified elastic gel. Optimal filling capacity for predictable, natural looking results whilst maintaining excellent tissue integration to minimize skin irregularities. Estimated duration: 12 months. Available with lidocaine (0.3%) and without lidocaine. |
| Estyme® FORM | Manufactured by Symatase; Distributed by Evolus, Inc | Indicated to correct nasolabial folds. | Injected into dermis to hypodermis. | 22 mg/ml cross-linked hyaluronic acid plus 0.3% lidocaine | 30G or 27G Needle (provided) 25G Cannula (not Provided) | Estyme is a next generation injectable hyaluronic acid made using Cold-X™ Technology by Symatase. |
| Estyme® SMOOTH | Manufactured by Symatase; Distributed by Evolus, Inc | Indicated to correct nasolabial folds and perioral lines. | Injected into dermis to hypodermis. | 20 mg/ml cross-linked hyaluronic acid plus 0.3% lidocaine | 30G Needle (provided) 25G Cannula (not Provided) | Estyme is a next generation injectable hyaluronic acid made using Cold-X™ Technology by Symatase. |
| HYABELL® Basic + Lidocaine | Adoderm GmbH | Correction of medium wrinkles. Lip volume and lip correction. | Medium to deep dermis | 16 mg/mL cross-linked hyaluronic acid plus 0.3 % lidocaine | Needle: 27 G | Exceptionally soft injection; and G' with 1Hz is lower than 70 Pa; for excellent properties in shaping and distribution, for stronger volume in the lips |
| Intense Flux | NEAUVIA® | Volume effect | Dermis | Hyaluronic acid content: 26 mg/ml Amino acids: Glycine & L-Proline Crosslinker: PEG (polyethylene glycol) | Needle: 27 G Canula: 30 G | Unique structural filler that combines PEGylated hyaluronic acid and 1% CaHA to form a dual effect scaffold that creates the perfect environment for physiological collagen production while being reversible. Due to its thermostable properties through PEG crosslinking, can be combined with NEAUVIA Energy-Based-Devices |
| Juvéderm® ULTRA 3 | Allergan | Mid and deep wrinkles, lip contour and lip volume | medium/ deep dermis | 24 mg/ml crosslinked HA (HYLACROSS-Technology™) | Needle: 27 G 1/2 | Smooth gel, duration nasolabial 12 months, with lidocaine (0.3 %) |
| Juvéderm® ULTRA 4 | Allergan | Deep wrinkles, volume creation in lips and cheeks | Deep dermis | 24 mg/mL crosslinked HA (HYLACROSS-Technology™) | Needle: 27 G 1/2 | Smooth gel, long duration with lidocaine (0.3 %) |
| Juvéderm® ULTRA SMILE | Allergan | Mid and deep wrinkles, lip contour and lip volume | medium/ deep dermis | 24 mg/mL crosslinked HA (HYLACROSS-Technology™) | Needle: 30 G 1/2 | Smooth gel, long duration with lidocaine (0.3 %) |

| Product name | Company | Indications | Application depth | Material i.e. hyaluronic acid concentration and crosslinkage | Needle and/or cannula size | Special material properties |
|--|--------------------------|---|--|--|---|---|
| Juvéderm® VOLBELLA with Lidocaine | Allergan | Superficial and medium-deep wrinkles, definition of lip contours | Upper and mid dermis | 15 mg/ml cross-linked HA, unique, patented VYCROSS Technology™, with long and short chain HA acids - for particularly fast tissue integration, long duration and low swelling of the gel | Needle: 30 G 1/2 | Good duration, good dispersion (reason: low cohesion), with lidocaine (0.3%). Results visible for up to 12 months |
| Juvéderm® VOLIFT | Allergan Inc. | Mid and deep wrinkles | Deep dermis (Recommendation: not intra dermal) | 17.5 mg/ml crosslinked HA (VYCROSS-Technology™), with long and short chain HA acids - for particularly fast tissue integration, long shelf life and low swelling of the gel | Needle: 30 G 1/2 | Good spreadability, contains lidocaine (0.3%), tissue proactive, results visible for up to 18 months |
| MaiLi Define | Sinclair Pharma | Facial reconstruction for congenital or disease-related structural defects: Scar tissue. Aesthetic treatment for pronounced skin depressions and lip augmentation | Deep dermis; subcutaneous or between mucosa and muscle | HA-Concentration: 18mg/ml | Needles: 4 x 30G/ packing unit | Ideal for filling deep wrinkles and recontouring the lips |
| My Filler Medium | My Med Aesthetics | Nasolabial folds, mentolabial folds (marionette lines), glabella and lip volume increase | Medium dermis | 25 mg/ml monophasic cross-linked HA. TRIO technology | Needle: 27 G or 30 G or Cannula | Easily spreadable gel with moderate lifting capacity |
| My Filler Glips | My Med Aesthetics | Specially developed for lips treatments such as volume and contouring as well mid face medium volumization. | Intra and subdermal | 20 mg/ml monophasic cross-linked HA and 5 mg/ml monophasic non-cross-linked HA. DUAL-Link technology | Needle: 27 G or 30 G or Cannula | Easily spreadable gel with moderate lifting capacity and immediately shining result. |
| PERFECTHA® Derm | Sinclair Pharma | Medium facial lines and skin depressions, glabellar lines, lip contour | Mid-dermis | 20 mg/g hyaluronic acid, cross linking agent BDDE (< 1%) | Needle: 30 G * 1/2" | E-Brid™-Technology; safe, well tolerated, easy to inject, high lifting and volumizing capacity, long lasting |
| PERFECTHA® Derm Lidocaine | Sinclair Pharma | Medium facial lines and skin depressions, glabellar lines, lip contour | Mid-dermis | 20 mg/g hyaluronic acid (non-animal, mixture of 90% cross-linked and 10% non-cross-linked hyaluronic acid), cross-linking agent BDDE (<1%) | Needle: 30 G x 13 mm | E-Brid™-Technology; safe, well tolerated, easy to inject, high lifting and volumizing capacity, long lasting |
| Restylane® Refyne™ | Galderma | Medium deep wrinkles (especially nasolabial & marionette wrinkles, tear-cheek-eyelid furrow) | Mid dermis | 20 mg/mL HA, gel with moderate crosslinkage and low calibration grade (Balance Technology) | Needle: 30 G 1/2 (UTWN) Canula: Steriglide (TSK) 27 G | Soft gel with moderate lifting capacity, with lidocaine |
| Restylane® Kysse™ | Galderma | Lip volume, lip contour | Lip vermilion, submucosa | 20 mg/mL HA, gel with moderate crosslinkage and low calibration grade (Balance Technology) | Needle: 30 G 1/2 (UTWN) Canula: Steriglide (TSK) 25-27 G | Moderate soft gel with moderate lifting capacity, available with lidocaine |
| Restylane® | Galderma | Medium deep wrinkles (especially nasolabial & marionette wrinkles, oral commissure), lip volume | Mid dermis | 20 mg/mL stabilized HA (NASHA Technology) | Needle: 29 G 1/2; Canula: 27 G Pixl™, 28 G Pixl+ | Firm gel with moderate lifting capacity, available with lidocaine |

| Product name | Company | Indications | Application depth | Material i.e. hyaluronic acid concentration and crosslinkage | Needle and/or cannula size | Special material properties |
|---------------------------------|----------------------------|---|-------------------------------------|--|---|--|
| Restylane® Lyft™ | Galderma | Deep wrinkles, slight to moderate facial contouring (especially nose, zygomatic region, chin, lower jaw contour) | Deep dermis or superficial subcutis | 20 mg/mL stabilized HA (NASHA Technology) | Needle: 29 G 1/2 (UTWN); Canula: 23–25 G Pixl™, 25 G Pixl+ | Firm gel with high lifting capacity, available with lidocaine |
| Revanesse® Ultra™+ | Prollenium | Brow, Temples, Submalar area, Nasolabial folds, & Marionette lines. Lip augmentation | Mid to deep dermis | 25 mg HA, 10% linear HA, Medium viscosity gel, Moderate Yield stress High cohesivity | 27 G | Next Generation HA Filler with proprietary Thixofix Technology and with Lidocaine. HMW HA chains. |
| saypha® FILLER | Croma-Pharma | The product is a visco-elastic solution for the correction of moderate to pronounced nasolabial folds. It is used for both cosmetic treatments and medical reconstructive applications, such as the treatment of facial lipotrophy, scars or morphological asymmetries. | Mid to deep dermis | HA concentration: 2.3% HA (23 mg/ml), Crosslinking degree: 0.5 - 1,0% | Needle: 2 x 27G 1/2" wall Terumo™ (CE 0197) | The Croma syringe - an innovation in terms of safety & comfort: High quality glass syringes are the gold standard with regard to extractables and leachables (E&L). In thorough tests Croma's high quality glass syringes showed a significantly better E&L profile than any plastic syringe. |
| saypha® FILLER Lidocaine | Croma-Pharma | The product is indicated for the correction of moderate to severe nasolabial folds and for the treatment of lips. | Mid to deep dermis and submucosa | HA concentration: 2.3% (23 mg/ml), Crosslinking degree: 0.5 - 1,0%, Lidocaine hydrochloride: 0,3% | Needle: 2 x 27G 1/2" wall Terumo™ (CE 0197) | Up to 9 months assumed residence time in the skin. In extensive tests, the high-quality glass syringes from Croma showed a significantly better E&L profile than any plastic syringe. Duration of effect of up to 9 months. |
| saypha® Lips Lidocaine | Croma-Pharma | The product is used to treat the lips (increase lip volume, improve lip contour and texture). | submucosa | HA concentration: 2.3% (23 mg/ml), Crosslinking degree: 0.5 -1,0%, Lidocaine hydrochloride: 0,3% | Needle: 2 x 27G 1/2" Needle thin wall Terumo™ (CE 0197) | The duration of effect is up to 6 months. In extensive tests, the high-quality glass syringes from Croma showed a significantly better E&L profile than any plastic syringe. Effective for up to 6 months. |
| Stimulate | NEAUVIA® | Replacement of fatty tissue volume in the area of the midface | | Hyaluronic acid content: 26 mg/ml Amino acids & CaHA: Glycine, L-Proline & 1 % CaHa Crosslinker: PEG (polyethylene glycol) | Needle: 21 G x 1 1/2" Canula: 22 G x 2" | "Unique structural filler that combines PEGylated hyaluronic acid and 1% CaHA to form a dual effect scaffold that creates the perfect environment for physiological collagen production while being reversible. Due to its thermostable properties through PEG crosslinking, can be combined with NEAUVIA Energy-Based-Devices" |
| Stimulate Man | NEAUVIA® | Replacement of fatty tissue volume in the area of the midface | | Hyaluronic acid content: 28 mg/ml Amino acids & CaHA: Glycine, L-Proline & 1 % CaHa Crosslinker: PEG (polyethylene glycol) | Needle: 21 G x 1 1/2" Canula: 22 G x 2" | Unique structural filler that combines PEGylated hyaluronic acid and 1% CaHA to form a dual effect scaffold that creates the perfect environment for physiological collagen production while being reversible. Due to its thermostable properties through PEG crosslinking, can be combined with NEAUVIA Energy-Based-Devices |
| STYLAGE® M | Laboratoires VIVACY | Correction of mid to deep wrinkles in the Nasolabial region and the cheek and chin region as well as the forehead | Mid to deep dermis | 20 mg IPN cross-linked HA with antioxidant manitol | Needles: 4 x 30 G 1/2" | IPN crosslinked HA with double 3D-matrix and antioxidant for reduction of possible swelling and hematomas. |

| Product name | Company | Indications | Application depth | Material i.e. hyaluronic acid concentration and crosslinkage | Needle and/or cannula size | Special material properties |
|---|---------------------|--|-----------------------|--|----------------------------|--|
| STYLAGE® M Lidocaine | Laboratoires VIVACY | Correction of mid to deep wrinkles in the Nasolabial region and the cheek and chin region as well as the forehead | Mid to deep dermis | 20 mg IPN cross-linked HA with antioxidant mannitol & lidocaine (0.3%) | Needles: 4 x 30 G 1/2" | IPN crosslinked HA with double 3D-matrix and antioxidant for reduction of possible swelling and hematomas |
| STYLAGE® L | Laboratoires VIVACY | Correction of very deep and pronounced wrinkles in the entire region of the face | Lower dermis | 24 mg IPN cross-linked HA with antioxidant mannitol | Needles: 4 x 27 G 1/2" | IPN crosslinked HA with double 3D-matrix and antioxidant for reduction of possible swelling and hematomas |
| STYLAGE® L Lidocaine | Laboratoires VIVACY | Correction of very deep and pronounced wrinkles in the entire region of the face | Lower dermis | 24 mg IPN cross-linked HA with antioxidant mannitol & lidocaine (0.3%) | Needles: 4 x 27 G 1/2" | IPN crosslinked HA with double 3D-matrix and antioxidant for reduction of possible swelling and hematomas |
| TEOSYAL RHA® 2 | TEOXANE | For the treatment of moderate, dynamic wrinkles and lips: Such as nasolabial and glabellar wrinkles, crow's feet, lip contours and subtle lip volume, as well as corner of the mouth and perioral wrinkles | Mid dermis, lips | Hyaluronic acid: non-crosslinked HMW-HA HA-concentration: 23 mg/ml | Needle: 30 G 1/2" | Latest generation of cross-linked hyaluronic acid filler: smooth gel with good elasticity for moderate wrinkles. Preserved Network Technology, for natural-looking results and a duration of action from 12 to 18 months. Syringe volume: 2 x 1 ml Lidocaine: 0.3% Degree of modification: ~ 3.1% |
| TEOSYAL® PURESENSE GLOBAL ACTION | TEOXANE | For the treatment of mild to moderate wrinkles. Such as glabella and nasolabial folds and marionette lines | Mid dermis | Hyaluronoc acid: cross-linked HA HA-concentration: 25 mg/ml | Needle: 30 G 1/2" | Monophasic gel with increased resistance to free radicals. The patented technology (OMPS) guarantees optimal cross-linking parameters within the manufacturing process, for a stable gel with good lifting capacity and can reach an efficiency of up to 18 months. Syringe volume: 2 x 1 ml Lidocaine: 0.3% Degree of modification: -6.5 |
| TEOSYAL RHA KISS® | TEOXANE | For the treatment of subtle lip volume, reinforcement of lip contours, corner of the mouth and perioral wrinkles, perfect for lip reshaping | Mid dermis, lips | Hyaluronic acid: Cross-linked HMW-HA. HA concentration: 23 mg/ml | Needle: 30 G x 1/2" | Latest generation of cross-linked hyaluronic acid filler: smooth gel with good elasticity for moderate wrinkles. Preserved Network Technology, for natural-looking results and a duration of action from 12 to 18 months. Syringe volume: 2 x 0.7 ml Lidocaine: 0.3% Degree of modification: ~ 3.1% |
| TEOSYAL RHA® 3 | TEOXANE | For the treatment of deep dynamic facial wrinkles: Nasolabial and marionette wrinkles, wrinkles at the corners of the mouth, lip contour enhancement, lip volume | Deep dermis, lips | Hyaluronic acid: Cross-linked HMW-HA. HA concentration: 23 mg/ml | Needle: 27 x G 1/2" | Latest generation of cross-linked hyaluronic acid filler: smooth gel with good elasticity for moderate wrinkles. Preserved Network Technology, for natural-looking results and a duration of action from 12 to 18 months. Syringe volume: 2 x 1 ml Lidocaine: 0.3% Degree of modification: ~ 3.6% |
| VARIODERM Lips & Medium | Adoderm GmbH | Lip contours, lip volume, moderate facial wrinkles | Medium to deep dermis | 16 mg/mL cross-linked hyaluronic acid plus 0.3% lidocaine | Needle: 27 G | Without lidocaine, exceptionally soft injection: intermediate value of 9N at G' and G'' lower than 50 Pa at 0.1 Hz. For moderate volume in the lips. |
| VARIODERM Basic | Adoderm GmbH | Medium facial folds in all areas, lip contouring | Medium to deep dermis | 12 mg/mL cross-linked hyaluronic acid. Approximate duration in the skin: 6 – 12 months | Needle: 27 G | Without lidocaine, exceptionally soft injection: intermediate value of 9 N at G' more than 250 Pa at 0.1 Hz. For a higher volume with less injection quantity. |

FILLERS FOR DEEP AUGMENTATION

| Product name | Company | Indications | Application depth | Material i.e. hyaluronic acid concentration and crosslinkage | Needle and/or cannula size | Special material properties |
|---|---|--|--|--|---|--|
| ART FILLER® UNIVERSAL 2 x 1.2ml | FILLMED Laboratoires | FILL & SHAPE: For the treatment of medium to deeper wrinkles + lips | Medium to deep dermis (+ mucosa) | 25 mg/ml cross-linked hyaluronic acid plus 0.3 % lidocaine | Needle: 4 x 27 G | TRI-HYAL® technology for natural results: Network of very long as well as long HA chains and free hyaluronic acid + optimized BDDE concentration |
| ART FILLER® LIPS 2 x 1ml | FILLMED Laboratoires | FILL & DEFINE: For the treatment of deeper wrinkles + lips | Deep dermis (+ mucosa) | 25 mg/ml cross-linked hyaluronic acid plus 0.3 % lidocaine | Needle: 4 x 27 G | TRI-HYAL® technology for natural results: Network of very long as well as long HA chains and free hyaluronic acid + optimized BDDE concentration |
| ART FILLER® VOLUME | FILLMED Laboratoires | VOLUMIZE & CONTOUR: To restore volume loss and facial contours | Deep dermis and subcutaneous to sup-raperiosteal | 25 mg/ml cross-linked hyaluronic acid plus 0.3 % lidocaine | Needle: 4 x 27 G | TRI-HYAL® technology for natural results: Network of very long as well as long HA chains and free hyaluronic acid + optimized BDDE concentration |
| Estyme® SCULPT | Manufactured by Symatase; Distributed by Evolus, Inc | Indicated to restore cheek volume loss. | Injected into hypodermis and supra-periosteal. | 23 mg/ml cross-linked hyaluronic acid plus 0.3% lidocaine | 27G Needle (provided) 25G Cannula (not Provided) | Estyme is a next generation injectable hyaluronic acid made using Cold-X™ Technology by Symatase. |
| BELOTERO® Intense | Merz Pharmaceuticals GmbH | Correction of deeper lines, such as nasolabial fold and marionette folds; lip volume. | Deep dermis | 25.5 mg/mL dynamically multi-crosslinked HA (CPM®-Technology) | Needle: 27 G 1/2 | High viscose polydensified elastic gel. Optimal filling capacity for predictable, natural looking results whilst maintaining excellent tissue integration to minimize skin irregularities. Estimated duration: 12 months. Available with lidocaine (0.3%) and without lidocaine. |
| BELOTERO® Volume | Merz Aesthetics | Volumizing cheeks, temples or chin or treating deep nasolabial folds; correcting signs of lipatrophy | Deep subcutaneous layers or above the periosteum | 26 mg/mL dynamically multi-cross-linked HA (CPM®-Technology) | Needle: 30 G 1/2; 27 G 1/2 Canula: 27 G/37 mm | High viscose polydensified, plastic gel. In comparison to other volumizers, well moldable and easy to inject. Estimated duration: up to 18 months. Very well tolerated. Available with lidocaine (0.3%) and without lidocaine. |
| HYABELL® Deep + Lidocaine | Adoderm GmbH | Correction of deep folds | deep dermis | 20 mg/mL cross-linked hyaluronic acid plus 0.3 % lidocaine. | Needle: 27 G | Exceptionally soft injection: 12 N at G' with more than 300 Pa at 01Hz. For a strong volume effect with medium aged patiens. |
| Intense LV | NEAUVIA® | Volume effect | | Hyaluronic acid content: 26 mg/ml Amino acids: Glycine & L-Proline Crosslinker: PEG (polyethylene glycol) | Needle: 21 G x2" Canula: 22 G x 1 1/2" | Has been developed to produce a filler that increases skin volume and at the same time has a high plasticity to add volume on the one hand and resist compression and deformation on the other. The product is malleable and can therefore be easily massaged in - for optimal results. Due to its thermostable properties through PEG cross-linking, can be combined with NEAUVIA Energy-Based-Devices |
| Juvéderm® ULTRA 4 | Allergan Inc. | Deep wrinkles, volume creation in lips and cheeks | Deep dermis | 24 mg/mL crosslinked HA (HYLACROSS-Technology™) | Needle: 27 G 1/2 | Smooth gel, long duration with lidocaine (0.3 %) |

| Product name | Company | Indications | Application depth | Material i.e. hyaluronic acid concentration and crosslinkage | Needle and/or cannula size | Special material properties |
|--|--------------------------|---|--|--|--------------------------------------|---|
| Juvéderm® VOLUMA with Lidocaine | Allergan Inc. | Volume creation in the mid-face | Supraperi- ostal | 20 mg/ml cross-linked HA, unique, patented VYCROSS Technology™, with long and short chain HA acids - for particularly fast tissue integration, long shelf life and low swelling of the gel | Needle: 27 G 1/2 | Very long efficacy up to 24 months, excellent tissue integration and collagen neogenesis with lidocaine (0.3 %) |
| Juvéderm® VOLIFT with Lidocaine | Allergan Inc. | Deep skin wrinkles, contour deficits, volume building of cheeks, chin and lips | Deep dermis (Recommendation: not intra dermal) | 17.5 mg/ml crosslinked HA (VYCROSS-Technology™), with long and short chain HA acids - for particularly fast tissue integration, long shelf life and low swelling of the gel | Needle: 30 G 1/2 | Good spreadability, contains lidocaine (0.3%), results visible for up to 18 months |
| My Filler Max | My Med Aesthetics | Correction of deep folds | Deep dermis and subdermal | 22 mg/ml monophasic cross-linked HA and 8 mg/ml monophasic non-cross-linked HA. DUAL-Link technology | Needle: 25 G or 27 G or cannula | High lifting capacity, medium-high viscosity, great volumization and immediately shining results. |
| My Filler Strong | My Med Aesthetics | Chin and cheek augmentation, jawline contour, delicate rhinoplastic and centre of the face | Deep dermis to the periosteum | 30 mg/ml monophasic cross-linked HA. TRIO technology | Needle: 25 G or 27 G or cannula | High lifting capacity, high viscosity and great volumization. |
| MaiLi Volume | Sinclair Pharma | Facial reconstruction for congenital or disease-related structural defects: Volume loss in HIV-associated lipodystrophy Aesthetic treatment of pronounced facial skin depressions. Volume augmentation of facial tissue | Subcutaneous fat tissue or supraperiosteal area | HA concentration 21mg/ml; 3mg/ml lidocaine | Needles: 4 x 30G/ packing unit | Designed for volume building in the face and subcutaneous injection into fat pads |
| PERFECTHA® Deep | Sinclair Pharma | Facial reconstruction for congenital or disease-related structural defects: Scar tissue. Aesthetic treatment for pronounced skin depressions and lip augmentation | Deep dermis; subcutaneous or between mucosa and muscle | HA-Concentration: 18mg/ml | Needles: 4 x 30G/ packing unit | Ideal for filling deep wrinkles and recontouring the lips |
| PERFECTHA® Deep Lidocaine | Sinclair Pharma | Lip volume, oral commissures | Deep dermis | 21 mg/g hyaluronic acid (non-animal, mixture of: 90% cross-linked and 10% non-cross-linked hyaluronic acid), cross-linking agent BDDE (<1%); 0.3% lidocaine | Needle: 27 G x 13 mm | E-Brid™-Technology; safe, well tolerated, easy to inject, high lifting and volumizing capacity, long lasting |

| Product name | Company | Indications | Application depth | Material i.e. hyaluronic acid concentration and crosslinkage | Needle and/or cannula size | Special material properties |
|-----------------------------|------------------------|---|--|--|--|--|
| Radiesse® | Merz Aesthetics | Nasolabial folds, augmentation of the cheeks, marionette lines, treatment of the jawline, augmentation of the hand to correct volume loss in the back of the hand, restoration and/or correction of fat tissue atrophy (lipoatrophy) in individuals suffering from the human immunodeficiency virus | Deep or sub-dermal tissue layer, near the subcutaneous structure | Filler on Basis 70 % gel-matrix, 30 % CaHa microspheres, 25-45 µm | Needle: 1.5cc: 2 x 27 G T.W. x 0.75" 0.4 x 20mm Terumo K-Pack Injection Needle 3cc: 2 x 25 G T.W. x 1.0" 0.5 x 25mm Terumo K-Pack Injection Needle | Immediate long-lasting results (12 months and longer) [4]. Very well suited for facial contour definition, vertical lifting and volume balancing due to high elasticity and viscosity; proven improvement of skin structure and skin firmness by physical induction of collagen, elastin, and angiogenesis; hardly any water-binding capacity, >200 clinical studies and scientific publications. Publications with >7500 patients on Radiesse®, available with lidocaine (0.3%) and without lidocaine |
| Restylane® Defyne™ | Galderma | Deep wrinkles, slight to moderate facial contouring (especially zygomatic region, chin, lower jaw contour) | Deep dermis or superficial subcutis | 20 mg/mL HA, gel with very high crosslinkage and high calibration grade (Balance Technology) | Needle: 27 G 1/2 (UTWN) Canula: Steriglide (TSK) 27 G | Moderate firm gel with high lifting capacity, available with lidocaine |
| Restylane® Lyft™ | Galderma | Deep wrinkles, facial contouring (especially zygomatic region, chin, lower jaw contour) | Deep dermis or superficial subcutis | 20 mg/mL stabilized HA (NASHA Technology) | Needle: 29 G 1/2; Canula: 23-25 G Pixl™, 25 G Pixl+ | Firm gel with high lifting capacity, available with lidocaine |
| Revanesse® Contour™+ | Prollenium | Medium to deep facial wrinkles Volume restoration and contouring | Deep dermis to subcutaneous | 25 mg cross-linked HA, 10% linear HA | 27 G | Next Generation HA Filler with proprietary Thixofix Technology and with Lidocaine. |
| Revanesse® Outline™+ | Prollenium | Medium to deep facial wrinkles Lip augmentation, Volume Restoration and contouring | Deep dermis to subcutaneous | 25 mg cross-linked HA gel, 4% linear HA | 29 G | Next Generation HA Filler with proprietary Thixofix Technology and with Lidocaine. |
| Revanesse® Shape™+ | Prollenium | Medium to deep facial wrinkles Lip augmentation, Volume Restoration and shap | Supraperiosteum | 25 mg cross-linked HA gel | 27 G | Next Generation HA Filler with proprietary Thixofix Technology and with Lidocaine. |
| saypha® VOLUME | Croma Pharma | The product is a viscoelastic solution for the correction of moderate to pronounced nasolabial folds. It is mainly used for cosmetic treatments, but can also be used for medical-reconstructive purposes, such as the treatment of facial lipoatrophy, disfiguring scars or morphological asymmetries. | Deep dermis or subcutis | HA concentration: 2.3% (23 mg/ml), Crosslinking degree: 0,5 -1,5% | Needle: 2 x 27G 1/2" Needle thin wall Terumo™ (CE 0197) | In extensive tests, the high-quality glass syringes from Croma showed a significantly better E&L profile than any plastic syringe. Duration of effect of up to 9 months. |

| Product name | Company | Indications | Application depth | Material i.e. hyaluronic acid concentration and crosslinkage | Needle and/or cannula size | Special material properties |
|--|----------------------------|--|--|---|---|---|
| saypha® VOLUME Lidocaine | Croma Pharma | The product is used to treat moderate to pronounced nasolabial folds. | Deep dermis or subcutis | HA concentration: 2.3% (23 mg/ml), Crosslinking degree: 0,5 -1,5%, Lidocaine hydrochloride: 0,3% | Needle: 2 x 27G 1/2" Needle thin wall Terumo™ (CE 0197) | The Croma syringe - an innovation in terms of safety and comfort: high-quality glass syringes are the gold standard in terms of extractables and leachables (E&L). In extensive tests, Croma's high-quality glass syringes showed a significantly better E&L profile than any plastic syringe. |
| saypha® VOLUME PLUS Lidocaine | Croma Pharma | The product is indicated for correcting moderate to pronounced volume deficits in the zygomatic-malar area of the midface, in the antero-medial cheek area and in the submalar region. It is administered by deep subcutaneous and/or supraperiosteal injection. | Deep subcutaneous and/or supraperiosteal | HA concentration: 2.5% (25 mg/ml), Crosslinking degree: 1,0 - 2,0%, Lidocaine hydrochloride: 0,3% | Needle: 2 x 27G 1/2" Needle thin wall Terumo™ (CE 0197) | In extensive tests, the high-quality glass syringes from Croma showed a significantly better E&L profile than any plastic syringe. Duration of action of up to 12 months. |
| STYLAGE® L | Laboratoires VIVACY | Correction of very deep and pronounced wrinkles in the entire region of the face | Lower dermis | 24 mg IPN cross-linked HA with antioxidant mannitol | Needles: 4 x 27 G 1/2" | IPN crosslinked HA with double 3D-matrix and antioxidant for reduction of possible swelling and hematomas. Also available with lidocaine (0.3 %) |
| STYLAGE® L Lidocaine | Laboratoires VIVACY | Correction of very deep and pronounced wrinkles in the entire region of the face | Lower dermis | 24 mg IPN cross-linked HA with antioxidant mannitol | Needles: 4 x 27 G 1/2" | IPN crosslinked HA with double 3D-matrix and antioxidant for reduction of possible swelling and hematomas |
| TEOSYAL® Deep Lines | TEOXANE | Deep lines / folds of the face | Deep dermis | 25 mg/mL crosslinked HA | Needle: 27 G 1/2 | Moderately viscous gel, also available with 0.3 % lidocaine. |
| TEOSYAL RHA® 3 | TEOXANE | For the treatment of deep dynamic facial wrinkles: Nasolabial and marionette wrinkles, wrinkles at the corners of the mouth, lip contour enhancement, lip volume | Deep dermis, lips | "Hyaluronic acid: Cross-linked HMW-HA. HA concentration: 23 mg/ml" | Needle: 27 x G 1/2" | Latest generation of cross-linked hyaluronic acid filler: smooth gel with good elasticity for moderate wrinkles. Preserved Network Technology, for natural-looking results and a duration of action from 12 to 18 months. Syringe volume: 2 x 1 ml Lidocaine: 0.3% Degree of modification: ~ 3.6% |
| TEOSYAL RHA® 4 | TEOXANE | Restoration of volume in large and dynamic areas of the face, cheek region around midface, contours/jawline and temples | Deep dermis, subcutaneous (superficial and deep fat compartments), preperiosteal | Hyaluronic acid: Cross-linked HMW-HA. HA concentration: 23 mg/ml" | Needle: 27 G x 1/2" | Neueste Generation des vernetzten Hyaluronsäurefillers: Formbares Gel mit sehr hohen Festigkeitseigenschaften und guter Elastizität für sanftes und dynamisches Volumen und eine definierte Konturierung größerer Bereiche. Preserved Network Technology für natürlich aussehende Ergebnisse mit hoher Elastizität und einer Wirkdauer von 15 bis zu 18 Monaten. Syringe volume: 2 x 1.2 ml Lidocaine: 0.3% Degree of modification: 4.0% |
| TEOSYAL® PURESENSE DEEP LINES | TEOXANE | Nasolabial folds, vertical lip lines, deep lines and wrinkles, cheek augmentation, restoration of the face shape | Mid and deep dermis, subcutaneous to preperiosteal | Hyaluronic acid: cross-linked HA. HA concentration: 25 mg/ml" | Needle: 27 G x 1/2" | Monophasic gel with increased resistance to free radicals. The patented technology (OMPS) guarantees optimal cross-linking parameters within the manufacturing process, for a stable gel with good lifting capacity and can reach an effect of up to 18 months. Syringe volume: 2 x 1 ml Lidocaine: 0.3% Degree of modification: -8% |
| VARIODERM Plus | Adoderm GmbH | Strongly defined facial folds. Moderate Volumising. | deep dermis | 18 mg/mL cross-linked hyaluronic acid. Approximate duration in the skin: 12-14 months. | Needle: 27 G | Exceptionally soft injection: 12 N at G´ over = 600 Pa at 0.1Hz to give great volume effect over 12 – 14 months. |

FILLERS FOR MAXIMUM DEEP AUGMENTATION

| Product name | Company | Indications | Application depth | Material i.e. hyaluronic acid concentration and crosslinkage | Needle and/or cannula size | Special material properties |
|-----------------------------------|---|---|--|--|---|--|
| ART FILLER® VOLUME | FILLMED Laboratoires | VOLUMIZE & CONTOUR: To restore volume loss and facial contours | Deep dermis and subcutaneous to supra-periosteal | 25 mg/ml cross-linked hyaluronic acid plus 0.3% lidocaine | Needle: 4 x 27 G | TRI-HYAL® technology for natural results: Network of very long as well as long HA chains and free hyaluronic acid + optimized BDDE concentration |
| BELOTERO® Volume | Merz Aesthetics | Volumizing cheeks, temples or chin or treating deep nasolabial folds; correcting signs of lipatrophy | Deep subcutaneous layers or above the periosteum | 26 mg/mL dynamically multi-crosslinked HA (CPM®-Technology) | Needle: 30 G; 27 G Canula: 27 G | Poly-densified, ductile gel. In comparison to other volumizers, well moldable. Estimated duration: up to 18 months. Very well tolerated. Available with lidocaine |
| ELLANSÉ® S | Sinclair Pharma | For contouring, shaping and correcting lines and wrinkles, as well as for volume augmentation. Treatment areas: temple and eyebrow area, cheekbone area, cheeks, nasolabial folds, lower jaw line, nose shaping, marionette lines, chin contouring | Subcutaneous, supra-periosteal | 70 % Carboxymethylcellulose (CMC), 30 % Synthetic polycaprolactone microspheres (PCL) | Needle: 27 G 3/4" | Collagen stimulator with immediate correction and subsequent volume building through biostimulation; longevity of 18 months. |
| ELLANSÉ® M | Sinclair Pharma | For contouring, forming and correction of lines and wrinkles as well as for volume augmentation. Treatment areas: temple and eyebrow areas, zygomatic bone, cheeks, nasolabial folds, mandibular line, nose, marionette lines, contouring of the chin | Subcutaneous, supra-periosteal | 70 % Carboxymethylcellulose (CMC), 30 % Synthetic polycaprolactone microspheres (PCL) | Needle: 27 G 3/4" | Collagen stimulator with instant correction and subsequent volume creation through bio stimulation; longevity of 24 months. |
| Estyme® SCULPT | Manufactured by Symatase; Distributed by Evolus, Inc | Indicated to restore cheek volume loss. | Injected into hypodermis and supra-periosteal. | 23 mg/ml cross-linked hyaluronic acid plus 0.3 % lidocaine | 27G Needle (provided) 25G Cannula (not Provided) | Estyme is a next generation injectable hyaluronic acid made using Cold-X™ Technology by Symatase. |
| HYABELL® Ultra + Lidocaine | Adoderm GmbH | Volumising and correction of deep folds. Facial contouring | Subdermal | 24 mg/mL cross-linked hyaluronic acid plus 0.3 % lidocaine. | Needle: 27 G | Exceptionally soft injection: 19N at G' more than 700 Pa. To achieve an excellent volume effect and lifting features of the skin. |
| Intense | NEAUVIA® | Structuring & Lifting | | Hyaluronic acid content: 28 mg/ml Amino acids: Glycine & L-Proline Crosslinker: PEG (polyethylene glycol) | Needle: 21 G x 2" Canula: 22 G x 1 1/2" | Due to its specific rheological properties - high cohesiveness, high plasticity and balanced viscoelastic properties - Intense acts like an implant. It remains where it is placed and produces a strong lifting effect. Due to its thermostable properties through PEG crosslinking, it can be combined with NEAUVIA Energy-Based-devices |
| Intense Man | NEAUVIA® | Structuring & Lifting | | Hyaluronic acid content: 28 mg/ml Amino acids: Glycine & L-Proline Crosslinker: PEG (polyethylene glycol) | Needle: 21 G x 2" Canula: 22 G x 1 1/2" | Due to its specific rheological properties - high cohesiveness, high plasticity and balanced viscoelastic properties - Intense acts like an implant. It remains where it is placed and produces a strong lifting effect. Due to its specific rheological properties - high cohesiveness, high plasticity and balanced viscoelastic properties - Intense acts like an implant. It remains where it is placed and produces a strong lifting effect. Due to its thermostable properties through PEG crosslinking, it can be combined with NEAUVIA Energy-Based-devices |

| Product name | Company | Indications | Application depth | Material i.e. hyaluronic acid concentration and crosslinkage | Needle and/or cannula size | Special material properties |
|--|-------------------|---|--|---|--|---|
| Juvéderm® ULTRA 4 | Allergan Inc. | Deep wrinkles, volume creation in lips and cheeks | Deep dermis | 24 mg/ml crosslinked HA (HYLACROSS-Technology™) | Needle: 27 G 1/2 | Smooth gel, long duration with lidocaine (0.3 %) |
| Juvéderm® VOLUMA with Lidocaine | Allergan Inc. | Volume creation in the mid-face | upper periosteal | 20 mg/ml crosslinked HA (VYCROSS-Technology™), with long and short chain HA acids - for particularly fast tissue integration, long shelf life and low swelling of the gel | Needle: 27 G 1/2 | Very long efficacy up to 24 months, excellent tissue integration and collagen neogenesis with lidocaine (0.3 %) |
| Juvéderm® VOLIFT with Lidocaine | Allergan Inc. | Deep skin wrinkles, contour deficits, volume building of cheeks, chin and lips | Deep dermis (Recommendation: not intra dermal) | 17.5 mg/ml crosslinked HA (VYCROSS-Technology™), with long and short chain HA acids - for particularly fast tissue integration, long shelf life and low swelling of the gel | Needle: 30 G 1/2 | Good spreadability, contains lidocaine (0.3%), results visible for up to 18 months |
| My Filler Strong | My Med Aesthetics | Chin and cheek augmentation, jawline contour, delicate rhinoplasty and centre of the face | Deep dermis to the periosteum | 30 mg/ml monophasic cross-linked HA. TRIO technology | Needle: 25 G or 27 G or cannula | High lifting capacity, high viscosity and great volumization. |
| MaiLi Extreme | Sinclair Pharma | Facial reconstruction of congenital or disease-related structural defects: Volume loss in HIV-associated lipodystrophy. Aesthetic treatment for facial volume restoration Volume augmentation of facial tissues. Adapted for supraperiosteal injection and volume restoration | Subcutaneous fat tissue or supraperiosteal area | HA concentration 24mg/ml 3mg/ml Lidocaine | Needle: 4 x 30G/per package unit | Most powerful of all MaiLi fillers for modeling and shaping the face |
| PERFECTHA® SubSkin | Sinclair Pharma | Facial contour modeling, volume building on cheeks and chin, hand rejuvenation | Subcutaneous or supraperiosteal | 20 mg/g hyaluronic acid (non-animal, mixture of 90 % cross-linked and 10% non-crosslinked hyaluronic acid), crosslinking agent BDDE (<1%) | Needle: 25 G x 13 mm | Long-lasting filler, hardly any water-binding properties, therefore suitable for areas prone to swelling, skin tightening, etc. |
| PERFECTHA® SubSkin Lidocaine | Sinclair Pharma | Facial contour modeling, volume building on cheeks and chin, hand rejuvenation | Subcutaneous or supraperiosteal | 20 mg/g hyaluronic acid (non-animal, mixture of 90 % cross-linked and 10% non-crosslinked hyaluronic acid), crosslinking agent BDDE (<1%) | Needle: 25 G x 13 mm | Long-lasting filler, hardly any water-binding properties, therefore suitable for areas prone to swelling, skin tightening, etc. |
| Radiesse® | Merz Aesthetics | Nasolabial folds, augmentation of the cheeks, marionette lines, treatment of the jawline, augmentation of the hand to correct volume loss in the back of the hand, restoration and/or correction of fat tissue atrophy (lipodystrophy) in individuals suffering from the human immunodeficiency virus | Deep or subdermal tissue layer, near the subcutaneous structure. | Filler on Basis 70 % gel-matrix, 30 % CaHa microspheres, 25-45 µm | Needle: 1.5cc: 2 x 27 G T.W. x 0.75" 0.4 x 20mm Terumo K-Pack Injection Needle 3cc: 2 x 25 G T.W. x 1.0" 0.5 x 25mm Terumo K-Pack Injection Needle | Immediate long-lasting results (12 months and longer) [4]. Very well suited for facial contour definition, vertical lifting and volume balancing due to high elasticity and viscosity; proven improvement of skin structure and skin firmness by physical induction of collagen, elastin, and angiogenesis; hardly any water-binding capacity, >200 clinical studies and scientific publications. Publications with >7,500 patients on Radiesse®, available with lidocaine (0.3%) and without lidocaine |

| Product name | Company | Indications | Application depth | Material i.e. hyaluronic acid concentration and crosslinkage | Needle and/or cannula size | Special material properties |
|--------------------------------------|----------------------------|--|---|---|---|---|
| Restylane® Volyme™ | Galderma | Volume build-up (especially temples, zygomatic region, lower jaw contour) | Subcutaneous to supra-periosteal | 20 mg/mLHA with high cross-linkage and high calibration grade (Balance Technology) | Needle: 27 G 1/2 (UTWN) Canula: Steriglide (TSK) 27 G | Moderate soft gel with very high lifting capacity, available with lidocaine |
| Revanesse® Pure™+ | Prolenium | Superficial and perioral lines and wrinkles. | Superficial dermis | 14 mg HA, 100% linear HA | 30 G | with Lidocaine |
| saypha® VOLUME PLUS Lidocaine | Croma Pharma | The product is indicated for correcting moderate to pronounced volume deficits in the zygomatic-malar area of the midface, in the antero-medial cheek area and in the submalar region. It is administered by deep subcutaneous and/or supraperiosteal injection. | Deep subcutaneous and/or supraperiosteal | HA concentration: 2.5% (25 mg/ml), Crosslinking degree: 1.0 - 2.0%, Lidocaine hydrochloride: 0.3% | Needle: 2 x 27G 1/2" Needle thin wall Terumo™ (CE 0197) | In extensive tests, the high-quality glass syringes glass syringes from Croma showed a significantly better E&L profile than any plastic syringe. Duration of action of up to 12 months. |
| SCULPTRA® | Sinclair Pharma | Volume creation of caved in areas, especially for correction of skin depressions such as lines wrinkles and scars | Subcutaneous, supra-periosteal | 150 mg Poly-L-lactic acid (PLLA), 90 mg sodium carboxymethyl cellulose, 1275 mg progene free mannitol | Needle: 26 G | Collagen stimulator with duration of up to 2 years |
| STYLAGE® XL | Laboratoires VIVACY | For volumetric lifting, volume extension of the cheek bones, treatment of facial contours and for treatment of fallen-in temples | Lower dermis til subcutaneous | 26 mg IPN cross-linked HA with antioxidant mannitol | Needle: 2 x 27 G 1/2", 2 x 23 G 11/4" | IPN crosslinked HA with double 3D-matrix and antioxidant for reduction of possible swelling and hematomas. |
| STYLAGE® XL Lidocaine | Laboratoires VIVACY | For volumetric lifting, volume extension of the cheek bones, treatment of facial contours and for treatment of fallen-in temples | Lower dermis til subcutaneous | 26 mg IPN cross-linked HA with antioxidant mannitol & lidocaine (0.3%) | Needle: 2 x 27 G 1/2", 2 x 23 G 11/4" | IPN crosslinked HA with double 3D-matrix and antioxidant for reduction of possible swelling and hematomas |
| STYLAGE® XXL | Laboratoires VIVACY | For volumetric lifting of large and very large volumene defects as well as lipoathropy | Subcutaneous | 21 mg IPN cross-linked HA with antioxidant mannitol, also available with lidocaine (0.3 %) | Needle: 2 x 21 G 1 1/2"; 1 x 21 G / 50 blunt cannula, pricker | HA with 0.3 % vasoconstrictive mepivacaine for reduction of eventual reddening and swelling |
| TEOSYAL RHA® 4 | TEOXANE | Restoration of volume in large and dynamic areas of the face, cheek region around midface, contours/jawline and temples | Deep dermis, subcutaneous (superficial and deep fat compartments), pre-periosteal | Hyaluronic acid: Cross-linked HMW-HA. HA concentration: 23 mg/ml | Needle: 27 G x 1/2" | Neueste Generation des vernetzten Hyaluronsäurefillers: Formbares Gel mit sehr hohen Festigkeitseigenschaften und guter Elastizität für sanftes und dynamisches Volumen und eine definierte Konturierung größerer Bereiche. Preserved Network Technology für natürlich aussehende Ergebnisse mit hoher Elastizität und einer Wirkdauer von 15 bis zu 18 Monaten. Syringe volume: 2 x 1.2 ml Lidocaine: 0.3% Degree of modification: 4.0% |

| Product name | Company | Indications | Application depth | Material i.e. hyaluronic acid concentration and crosslinkage | Needle and/or cannula size | Special material properties |
|--|---------------------|---|---------------------------------|---|--|--|
| TEOSYAL® PURESENSE ULTRA DEEP | TEOXANE | For the restoration of facial contours and volume building of the cheek region, chin and jawline and temples | Pre-periosteum | Hyaluronic acid: cross-linked HA. HA concentration: 25 mg/ml | Needle: 25 G 1/2" | The deep-acting TEOSYAL® PURESENSE ULTRA DEEP was specially developed for lifting & volume building. The duration of action is 12 to 18 months. Syringe volume: 2 x 1.2 ml Modification level: 10.0% Lidocaine: 0.3% |
| TEOSYAL® PURESENSE ULTIMATE | TEOXANE | For volume restoration of larger areas of the face: Cheeks/midface, remodeling of facial contours and chin and jawline | Subcutaneous and pre-periosteum | Hyaluronic acid: cross-linked HA. HA concentration: 22 mg/ml | Needle: 27G x 1/2" Canula: 23G x 1" | Monophasic gel with increased resistance to free radicals. The patented technology (OMPS) guarantees optimal cross-linking parameters within the manufacturing process, for a stable gel with good lifting capacity and can reach an efficiency of up to 18 months. Syringe volume: 2x 1ml Lidocaine: 0,3 % Modification level: -9 % |
| VARIODERM Subdermal | Adoderm GmbH | For optimum volumising at very deep folds. Ideal for Dorsum, facial contouring and male patients. | Subdermal | 27 mg/ml cross-linked hyaluronic acid. | Needle: 27 G | Exceptionally soft injection: 19 N at G' more than 2000 Pa. Longest duration volume effect with all fillers, more than 14 months with less injected product compared. Ideal when high volume is needed, male patients and facial contouring. |

SPECIAL INDICATION: SKINSURFACE, MESOTHERAPY AND SKINBOOSTERS

| Product name | Company | Indications | Application depth | Material i.e. hyaluronic acid concentration and crosslinkage | Needle and/or cannula size | Special material properties |
|-----------------------------|----------------------------|--|---------------------------|--|--|--|
| BELOTERO® Revive | Merz Aesthetics | Revitalize the skin, improve skin elasticity, skin firmness, UV-damaged skin and to balance fine and superficial wrinkles | Superficial to mid dermis | 20 mg/mL dynamically multi-cross-linked HA (CPM®-Technology) and 175 mg/ml glycerine | Needle: 30 G 1/2 | Polydensified, cohesive gel with glycerol, very good tissue integration. Beauty Booster with an immediate effect on skin hydration and skin roughness as well as a long term effect on skinelasticity and skin color. Very well tolerated, blanching technique possible. Estimated duration: 6-9 months. |
| DESIRIAL® | Laboratoires VIVACY | For intradermal injectionen in the genital area and for treatment of vaginal dryness and other symptoms of vulvo-vaginal atrophy | Depending on indication | 19 mg IPN cross-linked HA | Needle: 2 x 30 G 1/2" 2 x 27 G 1/2" | Desirial is the first worldwide HA product licensed for intradermal injectionen in the genital area and for treatment of vaginal dryness and other symptoms of vulvo-vaginal atrophy (CE) |
| HYABELL® Meso | Adoderm GmbH | Skinbooster, superficial folds, face, neck, décolleté, back of hand | Superficial dermis | 12,8 mg/ml not- cross-linked hyaluronic acid | Two 30 G disposable injection cannulas (1x4 mm, 1x13 mm) | Not-crosslinked HA for hydrating skin |

| Product name | Company | Indications | Application depth | Material i.e. hyaluronic acid concentration and crosslinkage | Needle and/or cannula size | Special material properties |
|--|-----------------------------|--|-------------------------|---|--|--|
| Hydro Deluxe | NEAUVIA® | Improvement of skin quality | Epidermis and dermis | Hyaluronic acid content: 18 mg/ml Amino acids & CaHA: Glycine, L-Proline & 0.01 % CaHa Crosslinker: Uncrosslinked HA | Needle: 4 x 30 G 1/2" | Contains 18 mg/ml of pure hyaluronic acid and is enriched with 0.01% calcium hydroxylapatite, glycine and L-proline. This unique composition creates the optimal environment for the physiological restoration of the skin |
| Hydro Deluxe Man | NEAUVIA® | Improvement of skin quality | Epidermis and dermis | Hyaluronic acid content: 18 mg/ml Amino acids & CaHA: Glycine, L-Proline & 0.01 % CaHa Crosslinker: Uncrosslinked HA | Needle: 4 x 30 G 1/2" | Contains 18 mg/ml of pure hyaluronic acid and is enriched with 0.01% calcium hydroxylapatite, glycine and L-proline. This unique composition creates the optimal environment for the physiological restoration of the skin |
| Juvéderm® HYDRATE | Allergan Inc. | Improvement of skin moisture and elasticity | Upper dermis | 13.5 mg/mL non-crosslinked HA with 0.9 % manitol | Needle: 30 G 1/6; 32 G | Good water binding capability, short duration |
| Juvéderm® VOLITE – Skin Juvénizer | Allergan Inc. | Improving skin quality factors moisture and elasticity. Smoothing fine wrinkles on the face, décolleté and hands | Intra dermal | 12 mg/ml cross-linked HA, unique, patented VYCROSS Technology™, with long- and short-chain HA acids - for particularly fast tissue integration, long shelf life and low swelling of the gel | Needle: 32G 1/2 | Only one application: results visible for up to 9 months. Significant hydration and patient satisfaction, contains lidocaine (0.3%) |
| M-HA® 10 3x3ml | FILLMED Laboratoires | For fine wrinkles, for hydration and radiance as well as elasticity. Especially also for face, neck, décolleté, back of the hand | Epidermis, upper dermis | 10 mg/ml hyaluronic acid | Needle: 3 x 30 G (12 mm) 3 x 32 G (4 mm) | An anti-aging solution for moisture, radiance and elasticity |
| My Filler HA Refil | My Med Aesthetics | Entire area of the face | Superficial dermis | 15 mg/ml monophasic cross-linked HA and 5 mg/ml monophasic non-cross-linked HA. DUAL-Link technology | Needle: 27 G, 30 G or 32 G | Very low viscosity with great hydration properties |
| My Filler HA Retouch | My Med Aesthetics | Entire area of the face. 2ml syringe. | Superficial dermis | 15 mg/ml monophasic cross-linked HA and 5 mg/ml monophasic non-cross-linked HA. DUAL-Link technology | Needle: 27 G, 30 G or 32 G | Very low viscosity with great hydration properties. 2 ml syringe. |
| NCTF® 135 HA 5x3ml | FILLMED Laboratoires | For fine wrinkles, hydration and skin thickening and a glow effect. Especially also for face, neck, décolleté, back of the hand | Epidermis, upper dermis | 5 mg/ml Hyaluronic Acid + Active ingredient complex: 12 vitamins + 24 amino acids + 6 co-enzymes + 5 nucleic acids + 6 minerals + 6 other substances | Needle: 5 x 30 G (12 mm) 5 x 32 G (4 mm) | Innovative formulation with hyaluronic acid and 60 active ingredients. Clinically proven complex of active ingredients |

| Product name | Company | Indications | Application depth | Material i.e. hyaluronic acid concentration and crosslinkage | Needle and/or cannula size | Special material properties |
|---|----------------------------|--|---------------------------------------|--|---|---|
| Restylane® Skinboosters™ Vital | Galderma | Improve skin hydration, skin texture and skin elasticity; requires more tissue coverage (thicker skin) | Dermis, preferably in its deep layers | 20 mg/ml stabilized HA (NASHA Technology) | 29 G TWN Smart Click System; 30 G PixL™ or Injector Pix'L 23 G, 50 mm und Pix'L 25 G, 40 mm | Strong water retention capability, well tolerated |
| Restylane® Skinboosters™ Vital Light | Galderma | Improve skin hydration, skin texture and skin elasticity; requires less tissue coverage (thinner skin) | Subcutaneous | 12 mg/ml stabilized HA (NASHA Technology) | 29 G TWN Smart Click System; 30 G PixL™ or Injector Pix'L 23 G, 50 mm und Pix'L 25 G, 40 mm | Strong water retention capability, well tolerated |
| Revitalize serums | My Med Aesthetics | Promotes skin repair and increases the rate of self-regeneration. | Superficial dermis | Revitalize Essence: Cross-linked HA Revitalize Pure: HA and Collagen. Revitalize Vitamins: 69 vitamins, peptides, etc. Revitalize Body: DMAE Revitalize Slim: phosphatidicoline Revitalize Hair: EGCG and DHQG Revitalize White Skin: Kolic Acid Revitalize Booster: Epidermal Growth Factor. | Microneedling, electroporation and meso techniques. | Organic, sterile and high quality with extreme beautiful results |
| saypha® RICH | Croma Pharma | The product is a viscoelastic solution and compensates for the loss of hyaluronic acid due to the aging process, moisturizes the skin, improves the tone and elasticity of the skin and fills small wrinkles such as crow's feet, smile lines or smoker's lines around the mouth | Superficial dermis | 1.8% (18 mg/ml) cross-linked HA, 2,0% Glycerin (20 mg/ml) | Needle: 2 x 30G 1/2" thin wall Terumo™ (CE 0197) | Glycerin (a polyalcohol) is a natural component of the skin. In extensive tests, the high-quality glass syringes from Croma showed a significantly better E&L profile than any plastic syringe. In saypha® RICH, it has a dual function: it protects the hyaluronic acid molecules from degradation while promoting skin hydration and elasticity |
| STYLAGE® Hydro | Laboratoires VIVACY | For mesotherapeutic treatments and restoration of skin moisture and improvement elasticity and firmness of the tissue | Superficial dermis | 14.0 mg non-crosslinked HA | Needle: 2 x 30 G 1/8" | Very long molecule chains (ca. 1.0 MDa-ton) for long durability |
| STYLAGE® HYDROMAX | Laboratoires VIVACY | For mesotherapy and intense hydration of the skin. Longlasting (4-6 Months) | Mid dermis | 12.5 mg lightly crosslinked HA with antioxidant sorbitol | Needle: 1 x 30 G 1/8" | Very high water binding capacity due to the antioxidant sorbitol |
| TEOSYAL PURESENSE REDENSITY® 1 | TEOXANE | Skinbooster to prevent signs of aging, hydration and densification of the skin. Improves the quality of the skin on the face, neck and décolleté | Superficial to mid dermis | Hyaluronic acid: non-cross-linked HMW-HA. HA concentration: 15 mg/ml" | Needle: 30 G 1/2" | Proven effectiveness through an exclusive patented formula with a combination of concentrated hyaluronic acid and essential nutrients that have a complementary effect. Syringe volume: 2 x 1 ml or 1 x 3 ml. Lidocaine: 0.3 % Modification level: 0% |

| Product name | Company | Indications | Application depth | Material i.e. hyaluronic acid concentration and crosslinkage | Needle and/or cannula size | Special material properties |
|---------------------------|---------------------|---|---------------------------|---|--|---|
| TEOSYAL RHA® 1 | TEOXANE | For the treatment of dynamic, superficial wrinkles on the face, neck and décolleté: In the perioral and periorbital areas, wrinkles of the forehead and neck, as well as to improvement of skin quality. Recommended in combination with REDENSITY® 1 for skin quality treatments (face, neck, décolleté) | Superficial to mid dermis | Hyaluronic acid: non-crosslinked HMW-HA HA-concentration: 15 mg/ml | Needle: 30 G 1/2" | Very sculptable gel with high elasticity for filling fine wrinkles on the face, neck and décolleté. Preserved Network Technology for natural-looking results and a duration of action of 12 months and longer. Syringe volume: 2 x 1 ml Lidocaine: 0.3% Degree of modification: ~ 1.9% |
| VARIODERM Mesolift | Adoderm GmbH | skinbooster, superficial folds, face, neck, décolleté, back of hand | superficial dermis | 12,8 mg/mL not-cross-linked hyaluronic acid, approximate duration in the skin 3 months. | Two 30 G disposable injection cannulas (2x4 mm, 2x13 mm) | Not-cross-linked HA for hydrating skin |

SPECIAL INDICATION: LIPS

| Product name | Company | Indications | Application depth | Material i.e. hyaluronic acid concentration and crosslinkage | Needle and/or cannula size | Special material properties |
|------------------------------------|---|---|---|---|--|--|
| ART FILLER® LIPS SOFT 1x1ml | FILLMED Laboratoires | SHAPING & HARMONIZING: For the treatment of lip contour, perioral wrinkles as well as for subtle lip volume | Mucosa (+ medium deep dermis) | 25 mg/ml cross-linked hyaluronic acid plus 0.3% lidocaine | Needle: 2 x 30 G | TRI-HYAL® technology for natural results: Network of very long as well as long HA chains and free hyaluronic acid + optimized BDDE concentration |
| ART FILLER® LIPS 2x1ml | FILLMED Laboratoires | FILL & DEFINE: For the treatment of deeper wrinkles + lips | Deep dermis (+ mucosa) | 25 mg/ml cross-linked hyaluronic acid plus 0.3% lidocaine | Needle: 4 x 27 G | TRI-HYAL® technology for natural results: Network of very long as well as long HA chains and free hyaluronic acid + optimized BDDE concentration |
| BELOTERO® Lips Shape | Merz Aesthetics | Lip volume, severe oral commissures | Mid to deep dermis. Submucosal | 25.5 mg/mL dynamically multi-crosslinked HA (CPM®-Technology) | Needle: 27 G 1/2 | |
| BELOTERO® Lips Contour | Merz Aesthetics | Lip contour, perioral lines, mild oral commissures | Superficial to mid-dermis and submucosal | 22.5 mg/mL dynamically multi-crosslinked HA (CPM®-Technology) | Needle: 27 G 1/2, 30 G 1/2 | Medium viscose polydensified cohesive gel. Filler does not dislocate in upon dynamic motion. Excellently suited for highly mobile areas. Good integration into tissue for smooth, natural results. Almost no water retention. Allows for superficial injections with limited complication risk. Blanching technique possible. Lidocaine (0.3%) included. |
| Estyme® LIPS | Manufactured by Symatase; Distributed by Evolus, Inc | Indicated to correct the volume and the shape of the lips | Injected into dermis, hypodermis and labial mucosa. | 20 mg/ml cross-linked hyaluronic acid plus 0.3% lidocaine | 30G Needle (provided) 25G Cannula (not Provided) | Estyme is a next generation injectable hyaluronic acid made using Cold-X™ Technology by Symatase. |

| Product name | Company | Indications | Application depth | Material i.e. hyaluronic acid concentration and crosslinkage | Needle and/or cannula size | Special material properties |
|---|-------------------------|---|--|--|--------------------------------|---|
| HYABELL® Lips + Lidocaine | Adoderm GmbH | Definition of lip contours, hydration of the lips | Intra and subdermal | 12 mg/ml cross-linked hyaluronic acid plus 0.3% lidocaine | Needle: 27 G | Exceptionally soft injection: intermediate value of 10 Nat G' and G'' with 0.1Hzis lower than 35 Pa; for excellent properties in shaping and distribution of the filler; for natural and elegant appearance of lip volume, low water uptake |
| Intense Lips | NEAUVIA® | Filling of wrinkles and fine lines | | Hyaluronic acid content: 24 mg/ml Amino acids: Glycine & L-Proline Crosslinker: PEG (polyethylene glycol) | Needle: 2 x 27 G 1/2" | |
| Juvéderm® ULTRA 3 | Allergan Inc. | Mid and deep wrinkles, lip contour and lip volume | lips mucosa | 24 mg/mL crosslinked HA (HYLACROSS-Technology™) | Needle: 27 G 1/2 | Smooth gel, duration nasolabial 12 months, with lidocaine (0.3 %) |
| Juvéderm® ULTRA 4 | Allergan Inc. | Deep wrinkles, volume creation in lips and cheeks | lips mucosa | 24 mg/mL crosslinked HA (HYLACROSS-Technology™) | Needle: 27 G 1/2 | Smooth gel, long duration with lidocaine (0.3 %) |
| Juvéderm® ULTRA SMILE | Allergan Inc. | Mid and deep wrinkles, lip contour and lip volume | Mid and deep dermis | 24 mg/mL crosslinked HA (HYLACROSS-Technology™) | Needle: 30 G 1/2 | Smooth gel, long duration with lidocaine (0.3 %) |
| Juvéderm® VOLBELLA with Lidocain | Allergan Inc. | Superficial and medium-deep skin wrinkles, definition of lip contours | Upper and mid dermis | 15 mg/ml crosslinked HA (HYLACROSS-Technology™, with long and short chain HA acids - for particularly fast tissue integration, long shelf life and low swelling of the gel | Needle: 30 G 1/2 | Good duration, good dispersion (reason: low cohesion), with lidocaine (0.3 %). Results visible for up to 12 months |
| Juvéderm® VOLIFT with Lidocaine | Allergan Inc. | Deep skin wrinkles, contour deficits, volume building of cheeks, chin and lips | Deep dermis (Recommendation: not intra dermal) | 175 mg/ml crosslinked HA (VYCROSS-Technology™), with long and short chain HA acids - for particularly fast tissue integration, long shelf life and low swelling of the gel | Needle: 30 G 1/2 | Good spreadability, contains lidocaine (0.3%), results visible for up to 18 months |
| MaiLi Define | Sinclair Pharma | "Facial reconstruction for congenital or disease-related structural defects: Scar tissue. Aesthetic treatment for pronounced skin depressions and lip augmentation" | Deep dermis; subcutaneous or between mucosa and muscle | HA-Concentration: 18mg/ml | Needles: 4 x 30G/ packing unit | Ideal for filling deep wrinkles and recontouring the lips |
| My Filler Glips | MyMed Aesthetics | Specially developed for lips treatments such as volume and contouring as well mid face medium volumization. | Intra and subdermal | 20 mg/ml mono-phasic cross-linked HA and 5 mg/ml mono-phasic non-cross-linked HA. DUAL-Link technology | Needle: 27 G, 30 G or Cannula | Easily spreadable gel with moderate lifting capacity and immediately shining result. |

| Product name | Company | Indications | Application depth | Material i.e. hyaluronic acid concentration and crosslinkage | Needle and/or cannula size | Special material properties |
|-----------------------------------|------------------------|---|---------------------------|--|---|--|
| PERFECTHA® Derm | Sinclair Pharma | Medium facial lines and skin depressions, glabellar lines, lip contour | Mid-dermis | 20 mg/g hyaluronic acid (non-animal, mixture of 90% cross-linked and 10% non-cross-linked hyaluronic acid), cross-linking agent BDDE (<1%) | Needle: 30 G x 13 mm | E-Brid™-Technology; safe, well tolerated, easy to inject, high lifting and volumizing capacity, long lasting |
| PERFECTHA® Derm Lido-caine | Sinclair Pharma | lip contour | Mid-dermis | "21 mg/g hyaluronic acid (non-animal, mixture of 90% cross-linked and 10% non-cross-linked hyaluronic acid), cross-linking agent BDDE (<1%)" | Needle: 30 G x 13 mm | E-Brid™-Technology; safe, well tolerated, easy to inject, high lifting and volumizing capacity, long lasting |
| PERFECTHA® Deep | Sinclair Pharma | Lip volume | Deep dermis | 20 mg/g hyaluronic acid (non-animal, mixture of 90% cross-linked and 10% non-cross-linked hyaluronic acid), cross-linking agent BDDE (<1%) | Needle: 27 G x 13 mm | E-Brid™-Technology; safe, well tolerated, easy to inject, high lifting and volumizing capacity, long lasting |
| PERFECTHA® Deep Lido-caine | Sinclair Pharma | Lip volume, oral commissures | Deep dermis | "21 mg/g hyaluronic acid (non-animal, mixture of 90% cross-linked and 10% non-cross-linked hyaluronic acid), cross-linking agent BDDE (<1%); 0.3% lidocaine" | Needle: 27 G x 13 mm | E-Brid™-Technology; safe, well tolerated, easy to inject, high lifting and volumizing capacity, long lasting |
| Restylane® Kysse™ | Galderma | Lip volume, lip contour | Lip vermilion, sub-mucosa | 20 mg/ml HA, gel with moderate crosslinkage and low calibration grade (Balance Technology) | Needle: 30 G 1/2 Canula: Steiriglide (TSK) 25 G bis 27 G | Moderate soft gel with moderate lifting capacity, available with lidocaine |
| Restylane® | Galderma | Correction of wrinkles and lip enhancement | Mid dermis | 20 mg/mL stabilized HA (NASHA Technology) | Needle: 29 G 1/2; Canula: 27 G Pixl™, 28 G Pixl+ | Firm gel with moderate lifting capacity, available with lidocaine |
| Revanesse® Kiss™+ | Prollenium | Lip augmentation, perioral lines, superficial lines and wrinkles | Superficial to mid dermis | 25 mg crosslinked HA gel, 10% linear HA | 27 G | Next Generation HA Filler with proprietary Thixofix Technology and with Lidocaine. |
| Revanesse® Ultra™+ | Prollenium | Moderate to severe facial wrinkles and folds. Volume restoration, lips augmentation, contouring | Mid to deep dermis | 25 mg cross-linked HA, 10% linear HA | 27 G | Next Generation HA Filler with proprietary Thixofix Technology and with Lidocaine. |

| Product name | Company | Indications | Application depth | Material i.e. hyaluronic acid concentration and crosslinkage | Needle and/or cannula size | Special material properties |
|---------------------------------|---|--|---|--|---|--|
| Revanesse® Outline™+ | Medium to deep facial wrinkles Lip augmentation, Volume Restoration and contouring | Deep dermis to subcutaneous | 25 mg cross-linked HA gel, 4% linear HA | 29 G | with Lidocaine | Next Generation HA Filler with proprietary Thixofix Technology and with Lidocaine. |
| saypha® FILLER Lidocaine | Croma Pharma | The product is indicated for the correction of moderate to severe nasolabial folds and to increase lip volume. | Mid to deep dermis and submucosa | 2.3% (23 mg/ml) cross-linked HA, 0.3% lidocaine hydrochloride | Needle: 2 x 27G 1/2" Needle thin wall Terumo™ (CE 0197) | The duration of effect is up to 9 months. In extensive tests, the high-quality glass syringes from Croma showed a significantly better E&L profile than any plastic syringe. |
| saypha® Lips Lidocaine | Croma Pharma | The product is used to treat the lips (increase lip volume, improve lip contour and texture). | submucosa | HA concentration: 2.3% (23 mg/ml), Crosslinking degree: 0.5 -1.0%, Lidocaine hydrochloride: 0.3% | Needle: 2 x 27G 1/2" Needle thin wall Terumo™ (CE 0197) | The duration of effect is up to 6 months. In extensive tests, the high-quality glass syringes from Croma showed a significantly better E&L profile than any plastic syringe. Effective for up to 6 months. |
| STYLAGE® LIPS | Laboratoires VIVACY | Lip volume, correction of disproportional upper and lower lips, definition and/or correction of lip contour, filling of fine lines above the upper lip, restoration of lip moisture | Lip mucosa | 18.5 mg IPN crosslinked HA with antioxidant mannitol | Needle: 2 x 30 G 1/2" | Estimated duration: ca. 12 months |
| STYLAGE® LIPS Lidocaine | Laboratoires VIVACY | Lip volume, correction of disproportional upper and lower lips, definition and/or correction of lip contour, filling of fine lines above the upper lip, restoration of lip moisture | Lip mucosa | 18.5 mg IPN cross-linked HA with antioxidant mannitol & lidocaine (0.3%) | Needle: 2 x 30 G 1/2" | Estimated duration: ca. 12 months |
| STYLAGE® LIPS PLUS | Laboratoires VIVACY | STYLAGE® Lips Plus is designed to give significantly more volume to the red of the lips. The product can be used for total lip treatment: Lip augmentation, treatment of drooping corners of the mouth and redefinition of the lip contour | Lip mucosa | 20 mg IPN cross-linked HA with antioxidant mannitol & lidocaine (0.3%) | Needle: 2 x 30 G 1/2" | Estimated duration: ca. 12 months |
| STYLAGE® M | Laboratoires VIVACY | Correction of mid to deep wrinkles in the Nasolabial region and the cheek and chin region as well as the forehead | Mid to deep dermis | 20 mg IPN cross-linked HA with antioxidant mannitol | Needles: 4 x 30 G 1/2" | IPN crosslinked HA with double 3D-matrix and antioxidant for reduction of possible swelling and hematomas |
| STYLAGE® M Lidocaine | Laboratoires VIVACY | Correction of mid to deep wrinkles in the Nasolabial region and the cheek and chin region as well as the forehead | Mid to deep dermis | 20 mg IPN cross-linked HA with antioxidant mannitol & lidocaine (0.3%) | Needles: 4 x 30 G 1/2" | IPN crosslinked HA with double 3D-matrix and antioxidant for reduction of possible swelling and hematomas |
| STYLAGE® L | Laboratoires VIVACY | Correction of very deep and pronounced wrinkles in the entire region of the face | Lower dermis | 24 mg IPN crosslinked HA with antioxidant mannitol | Needles: 4 x 27 G 1/2" | IPN crosslinked HA with double 3D-matrix and antioxidant for reduction of possible swelling and hematomas |

| Product name | Company | Indications | Application depth | Material i.e. hyaluronic acid concentration and crosslinkage | Needle and/or cannula size | Special material properties |
|--------------------------------|----------------------------|--|-------------------|---|----------------------------|---|
| STYLAGE® L | Laboratoires VIVACY | Correction of very deep and pronounced wrinkles in the entire region of the face | Lower dermis | 24 mg IPN cross-linked HA with antioxidant manitol & lidocaine (0.3%) | Needles: 4 x 27 G 1/2" | IPN crosslinked HA with double 3D-matrix and antioxidant for reduction of possible swelling and hematomas |
| TEOSYAL RHA® 2 | TEOXANE | "For the treatment of moderate, dynamic wrinkles and lips: Such as nasolabial and glabellar wrinkles, crow's feet, lip contours and subtle lip volume, as well as corner of the mouth and perioral wrinkles" | Mid dermis, lips | Hyaluronic acid: non-crosslinked HMW-HA HA-concentration: 23 mg/ml | Needle: 30 G 1/2" | Latest generation of cross-linked hyaluronic acid filler: smooth gel with good elasticity for moderate wrinkles. Preserved Network Technology, for natural-looking results and a duration of action from 12 to 18 months. Syringe volume: 2 x 1 ml Lidocaine: 0.3% Degree of modification: ~ 31% |
| TEOSYAL RHA KISS® | TEOXANE | For the treatment of subtle lip volume, reinforcement of lip contours, corner of the mouth and perioral wrinkles, perfect for lip reshaping | Mid dermis, lips | Hyaluronic acid: Cross-linked HMW-HA. HA concentration: 23 mg/ml | Needle: 30 G x 1/2" | Latest generation of cross-linked hyaluronic acid filler: smooth gel with good elasticity for moderate wrinkles. Preserved Network Technology, for natural-looking results and a duration of action from 12 to 18 months. Syringe volume: 2 x 0.7 ml Lidocaine: 0.3% Degree of modification: ~ 31% |
| TEOSYAL RHA® 3 | TEOXANE | For the treatment of deep dynamic facial wrinkles: Nasolabial and marionette wrinkles, wrinkles at the corners of the mouth, lip contour enhancement, lip volume | Deep dermis, lips | Hyaluronic acid: Cross-linked HMW-HA. HA concentration: 23 mg/ml | Needle: 27 x G 1/2" | Latest generation of cross-linked hyaluronic acid filler: smooth gel with good elasticity for moderate wrinkles. Preserved Network Technology, for natural-looking results and a duration of action from 12 to 18 months. Syringe volume: 2 x 1 ml Lidocaine: 0.3% Degree of modification: ~ 3.6% |
| TEOSYAL PURESENSE KISS® | TEOXANE | For a pronounced increase in lip volume, strengthening of lip contours, wrinkles at the corners of the mouth | Deep dermis, lips | Hyaluronic acid: Cross-linked HA. HA concentration: 25 mg/ml | Needle: 27 G 1/2" | Firm gel for a pronounced lip volume. Preserved Network Technology for natural-looking results with high elasticity and an effective duration of 12 up to 18 months. Syringe volume: 2 x 1 ml Lidocaine: 0.3% Modification level: 8% |

SPECIAL INDICATION: UNDER EYE/TEAR TROUGH

| Product name | Company | Indications | Application depth | Material i.e. hyaluronic acid concentration and crosslinkage | Needle and/or cannula size | Special material properties |
|---------------------------------------|-------------------|---|----------------------------|--|--|---|
| Restylane® Eyelight™ | Galderma | Tear trough, Dark Eye circles | supra periosteal | 20 mg/ml stabilized HA, (NASHA Technology) | Needle: 29 G Canula: Pix'L 27G, oder Pix'L 28 G | Moderate soft gel with moderate lifting capacity, available with lidocaine |
| Revanesse® Revise™+ | Prollenium | Superficial to moderate lines and wrinkles, volume restoration, lip augmentation, skin hydration and contouring of depressions | Superficial to mid dermis | 12 mg cross-linked HA gel | 30 G | Next Generation HA Filler with proprietary Thixofix Technology and with Lidocaine. |
| TEOSYAL PURESENSE REDENSITY® 2 | TEOXANE | Specially designed for the correction of tear trough and cheek lid furrow, low pronounced lower eyelid bags and zygomatic folds | Deep dermis, preperiosteum | Hyaluronic acid: combination of non-cross-linked and cross-linked HMW-HA. HA concentration: 15 mg/ml" | Needle: 30 G 1/2" | First and specially developed HA filler for tear trough and the entire perioral region. Unique combination of cross-linked and non-cross-linked hyaluronic acid, essential nutrients that have a complementary effect, with an effective duration of up to 12 months. Syringe volume: 2 x 1 ml Lidocaine: 0.3% Modification level: 5,5% |

SPECIAL INDICATION: VAGINAL REJUVENATION

| Product name | Company | Indications | Application depth | Material i.e. hyaluronic acid concentration and crosslinkage | Needle and/or cannula size | Special material properties |
|-----------------------|----------------------------|---|-------------------------|---|--|---|
| DESIRIAL® | Laboratoires VIVACY | For intradermal injections in the vaginal area and for treatment of vaginal dryness and other symptoms of vulvo-vaginal atrophy | Depending on indication | 19 mg IPN cross-linked HA | Needle: 2 x 30 G 1/2", 2 x 27 G 1/2" | Desirial is the first worldwide HA product licensed for intradermal injections in the genital area and for treatment of vaginal dryness and other symptoms of vulvo-vaginal atrophy (CE) |
| DESIRIAL® PLUS | Laboratoires VIVACY | Certified for vaginal surgical, volumetric treatments (i.e. clitoris and g-spot injections, labial modelling) | Depending on indication | 21 mg IPN cross-linked HA | Needle: 2 x 30 G 1/2", 1 x 18 G 80 blunt cannula | Polydensified, plastic gel. Compared to other volumizers, well modable |
| Intense Rose | NEAUVIA® | Rejuvenation of the intimate area | | Hyaluronic acid content: 28 mg/ml Amino acids: Glycine & L-Proline Crosslinker: PEG (polyethylene glycol) | Needle: 21 G x 40 mm Canula: 22 G x 50 mm | Has been developed with the highest possible concentration of hyaluronic acid in the NEAUVIA product range: 28 mg/mL. Infiltration into the labia majora can produce a significant rejuvenating effect. Volume, tightening and shape correction are performed together in a simple outpatient procedure. Can be combined with NEAUVIA Energy-Based- devices due to its thermostable properties through PEG cross-linking |

| Product name | Company | Indications | Application depth | Material i.e. hyaluronic acid concentration and crosslinkage | Needle and/or cannula size | Special material properties |
|------------------|-----------------|--|----------------------------|--|----------------------------|-----------------------------------|
| Sculptra® | Galderma | Skin aging / skin sagging and loss of volume | intra dermal, subcutaneous | Poly-L-lactic acid (PLLA; 150 mg) | Needle: 26 G | Biodegradable collagen stimulator |

SPECIAL INDICATION: BIOSTIMULATION

| Product name | Company | Indications | Application depth | Material i.e. hyaluronic acid concentration and crosslinkage | Needle and/or cannula size | Special material properties |
|-----------------------------|-------------------------|--|--------------------|---|------------------------------|---|
| My Filler HA Refil | MyMed Aesthetics | Entire area of the face | Superficial dermis | 15 mg/ml monophasic cross-linked HA and 5 mg/ml monophasic non-cross-linked HA DUAL-Link technology | Needle: 27 G or 30 G or 32 G | Very low viscosity with great hydration properties |
| Revanesse® Pure™+ | Prollenium | Forehead, emerging lines and perioral lines. | Superficial dermis | "14 mg HA, 100% linear HA, very low cohesivity" | 30 G | Next Generation HA Filler with proprietary Thixofix Technology and with Lidocaine. HMW HA chains. |
| My Filler HA Retouch | MyMed Aesthetics | Entire area of the face. 2ml syringe. | Superficial dermis | 15 mg/ml monophasic cross-linked HA and 5 mg/ml monophasic non-cross-linked HA DUAL-Link technology | Needle: 27 G or 30G or 32 G | Very low viscosity with great hydration properties. 2 ml syringe. |

SPECIAL INDICATION: GLUTEAL AUGMENTATION

| Product name | Company | Indications | Application depth | Material i.e. hyaluronic acid concentration and crosslinkage | Needle and/or cannula size | Special material properties |
|--|---------------------|-----------------------------|-----------------------------------|--|--|--|
| VARIOFILL® for gluteal augmentation | Adoderm GmbH | buttock lift and contouring | Subdermal layer in the fat tissue | 33 mg/ml cross-linked hyaluronic acid | Blunt rigid cannula (recommended 14G or wider diameter) Not included in the box. | G': 1784 Pa at 100 rad/s G'': 708 Pa at 100 rad/s Highly cohesive gel 3 years shelf life keeping its rheological properties Up to 24 months duration 100% designed, made and certified in Germany |

FILLER COMPANYS

The Filler Guide including the listed data is not exhaustive. For current and continuative information, the websites of the manufacturers should be visited, which we have listed here:

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INTERVIEW

PLLA as a Biostimulator

What do we know and what should patients be informed about?

Cosmetic Medicine interviewed Dr. Stanislaus Wüst, author of the recently published manuscript on the molecular mechanism of PLLA (<https://doi.org/10.1111/jocd.16635>) and Dr. Flavia Radke, a long-standing PLLA user and trainer, on the latest data and patient communication in the field of biostimulators. The interview partners stated before the start of the interview that all terms used are to be considered gender-neutral.

CM: Dr. Wüst, you recently published a manuscript together with Dr. Avelar and Dr. Nabhani in which you report on new findings regarding the mechanism of action of poly-L-lactic acid in its role as a Biostimulator. A lot has obviously happened in this field in recent years. Can you please summarise the most important points for us?

Dr. Wüst: Yes, the field is very dynamic. PLLA has been used as a biostimulator in aesthetic medicine for 25 years. In this case a suspension of PLLA particles in the micrometer range is injected subdermally. Over time, the particles are absorbed by the body. Until now, research has assumed that the biostimulating effect is mainly caused by a foreign body reaction and a resulting controlled inflammatory response. However, from a holistic point of view, this is only part of the process. The latest publications in the field



Fig. 1: Dr. Flavia Radke

suggest that PLLA directly activates various cell types. PLLA alone – that is, without the help of the immune system – causes fibroblasts to synthesize collagen and elastin and thus rebuild the extracellular matrix. On the other hand, there are the macrophages of the immune system. We assume that they go into M2 polarization through contact with PLLA. This means that they have an anti-inflammatory effect and, above all, promote regeneration. This happens, for example, through the release of TGF- β , a signaling molecule that promotes, among other things, fibroblast growth and adipogenesis. In addition, M2 polarized macrophages secrete interleukins 4 and 13, which are also signaling molecules that promote tissue regeneration. We also have clear indications

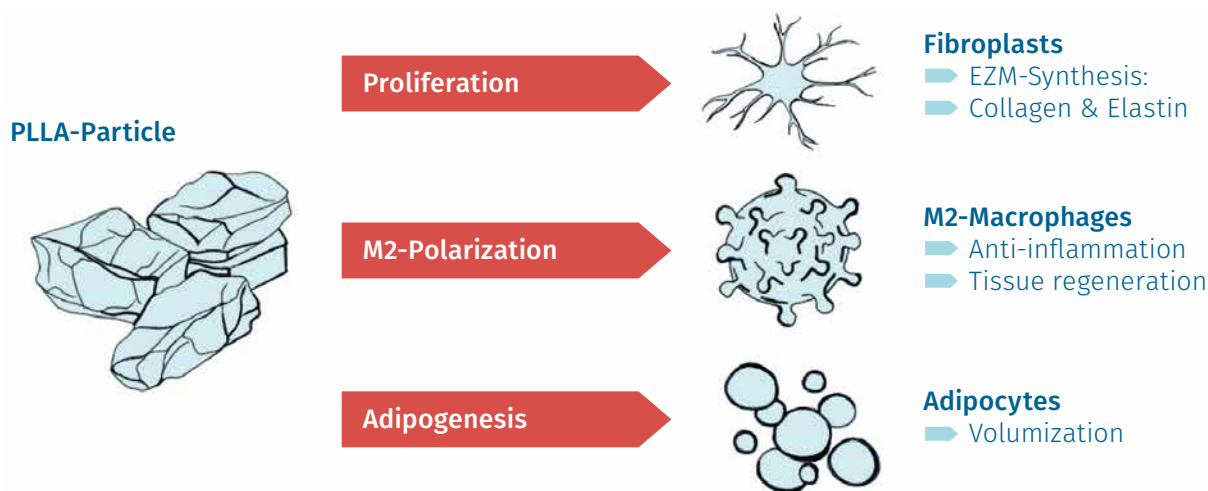


Fig. 2: Dr. Stas Wüst

that PLLA directly boosts adipogenesis and can therefore directly control volume build-up. These findings are also supported by the SPLASH study which was recently published by Dr. Sabrina Fabi and documented a significant volume increase in hip dips after the application of PLLA. In my opinion, these are the main findings of our publication. Even if not all molecular and physiological relationships can be fully explained at this point, based on the available data we can say that the effect of PLLA is anti-inflammatory. It suppresses inflammation and promotes tissue regeneration.

CM: Thank you very much, Dr. Wüst. So you are talking about a change of hypothesis in the molecular mechanism of PLLA. But let's now

FIG. 1: THE EFFECT OF PLLA ON VARIOUS CELL TYPES IN THE SKIN.



try to apply these findings to everyday practice. Dr. Radke, you have been following the development of the manuscript with great interest. You are in close scientific contact with Dr. Wüst and have thus been able to gain a good insight into the new findings. As a plastic surgeon and trainer in the field of injectables, you work a lot with patients but also with medical colleagues. Can you summarise for our readers how patient communication should now be adapted?

Dr. Radke: In my opinion, the most important point is and remains that patients are well informed, have considered the therapy and can then consciously decide for or against a treatment. The increasing scientific data is essential for this. With regard to patient communication by colleagues working in the field of aesthetics, I would also recommend addressing the mechanism of action. The published data provides us with an excellent template for this. I would describe the mechanism of action to the patient something like this:

1. The effect of a biostimulator is slow to take hold. It takes several weeks before the first results become visible. However, these will look more

natural because the body's own tissue is being built up. This explanation is essential because patients are accustomed to receiving faster visible effects from other therapies. Managing expectations is particularly important here.

2. PLLA promotes regeneration at a variety of levels and has an anti-inflammatory effect. The effect is localised and can be controlled by the injector.

3. PLLA activates various cell types in our skin and thus affects the entire extracellular matrix:

a. Skin fibroblasts. Cells that are responsible for producing the connective tissue of the skin multiply and rebuild the connective tissue after coming into contact with PLLA.

b. Macrophages. Immune system cells that decide on inflammation (e.g. redness) of the skin change their programme after contact with PLLA. They send out signals that suppress inflammation and promote tissue growth.

c. Pre-adipocytes. The precursors of fat cells form new fatty tissue after stimulation by PLLA. Depending on the treated area, this can have a volumising effect.

d. The cells communicate with each other, further increasing the growth effects.

Based on Dr. Wüst's publication, I have also developed a graphic representation that simplifies the processes. It will be published with the interview. Finally, I would like to emphasise the importance of patient education. In this context, the patient must be made aware of the possible side effects. It should also be clearly communicated what the limitations of the treatment are. For example, PLLA can reduce skin laxity, but it cannot remove excess tissue.

CM: This is very helpful for physicians and improves the quality of the information. Thank you. Finally, could you both give us a brief overview of the future of PLLA in aesthetics? What does the future hold for us?

Dr. Wüst: The developments in this field are really exciting. I think that we will see a lot of far-reaching discoveries in the coming years. One of the main aspects is the question of how the biostimulating effect is actually mediated. The group around Wen Jin, Kai Li and Wei Cai provided us with a first clue by identifying the molecular lactate transporter Mct1/4 as one of the main regulators for PLLA-mediated effects. I can

imagine that the activation of such molecules and of biostimulating signalling pathways in general will be an important pillar of regenerative medicine and will grow far beyond pure aesthetics.

I would also like to mention the work of the group led by Suichi Ogino and Naoki Morimoto. The group is working on adipogenesis and has been able to show in various animal models how PLLA implants influence fat growth. I strongly suspect that we will soon also see biostimulating PLLA implants in reconstructive breast surgery.

As for injectable PLLA implants, I think that I will continue to see a general upward trend in the use of Biostimulators in aesthetics. Biostimulants and especially PLLA have become an integral part of aesthetic portfolios.

Dr. Radke: I think that we are still at the very beginning with biostimulation and especially with PLLA. Although the products have been known for 25 years, their use in aesthetics is not yet widespread in Germany. This is shown by current market analyses. In recent years,

new treatment areas have been approved, where different therapy effects have been achieved. In some areas, it tends to improve adhesion and thus tighten tissue, while in others, it tends to increase volume after collagen biostimulation. The latest published studies show that the complete scope of the mechanism of action has not yet been fully determined. A few years ago, we did not even think about M2 polarisation and thus a complete regeneration cascade. Therefore, further research in this area is certainly very interesting and promising. I think there are also many other aspects whose effects should be investigated more intensively, such as the type of injection and how it is performed. Is there an advantage of the sharp injection over the blunt technique?

As far as product development is concerned, it would be interesting to know whether there is a PLLA-SCA formulation that does not require reconstitution. We have already seen a similar development in neuromodulators. This would have a high impact in terms of patient safety due to more precise dosing and error prevention. In any case, I am

ABOUT THE AUTHORS:

Dr. Flavia Radke is a consultant in plastic and aesthetic surgery and has been working in this field for 15 years. As an aesthetic expert and international trainer, she also trains doctors in the field of conservative aesthetics and is actively involved in scientific research.

Dr. Stanislaus Wüst is an independent consultant with industry experience as a medical science liaison in aesthetic dermatology and as a project manager for clinical studies. As a scientist, Dr. Wüst focused on research into the ageing process in the musculature at the Max Planck Institute for Heart and Lung Research, Brandeis University and the Max Planck Institute for Biology of Ageing.

very excited about future developments in biostimulation.

CM: Dr. Radke, Dr. Wüst, thank you very much for this fascinating interview.

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Safety through training in aesthetic medicine

AN INTERVIEW WITH DR. SAID HILTON, PRESIDENT OF THE DGBT – GERMAN SOCIETY OF AESTHETIC BOTULINUM AND FILLER THERAPY AND DR. TANJA FISCHER, PRESIDENT OF ISAC – INTERNATIONAL SOCIETY FOR AESTHETIC COMPETENCE



Fig. 1: Tanja Fischer, M.D.



Fig. 2: Said Hilton, M.D.

Aesthetic medicine is experiencing unprecedented demand. With this growing number of treatments with fillers, the side effects are also increasing. In particular, vascular complications – including blindness – can pose immense challenges for doctors in terms of patient safety. We spoke with Dr. Said Hilton, president of the German Society for Aesthetic Botulinum and Filler Therapy (DGBT), and Dr. Tanja Fischer, president of the International Society for Aesthetic Competence (ISAC), about the importance of training and safety training in aesthetic medicine, as well as the effects of the production cessation of the antidote Hylase Dessau.

CM: Dr. Hilton, why is training so important in aesthetic medicine, particularly in the area of hyaluronic acid and botulinum toxin?

S. Hilton: Aesthetic medicine is a highly complex discipline that requires anatomical knowledge, which must be analysed and applied individually to each patient, and precise knowledge of the products used. A wrongly placed injection can lead not only to aesthetic complications, but also to life-changing ones. The DGBT has made it its mission to train doctors to the highest standards, not only in technique, but also in risk assessment and the prevention of side effects.

CM: Dr. Fischer, how does an ISAC I-secure emergency course work, and why are these training sessions so crucial for patient safety?

T. Fischer: Our emergency courses prepare doctors for an emergency. It's not just about recognising

vascular occlusions, but also knowing how to react immediately. We have developed a consensus with our international ISAC World Board. Because we face the same challenges all over the world. Young doctors are now afraid of vascular occlusions, but fear is a poor companion. Many non-specialist groups, such as alternative practitioners, are fearlessly active in this market and are unable to recognise or adequately treat the side effects. In our courses, the therapy algorithm is explained according to the international consensus. We simulate real-life scenarios – from a mild occlusion to blindness. Participants have to react quickly, because in real life, the right action can determine the outcome of the adverse reaction.

Example:

A doctor recently reported on a patient who, after a rhinoplasty with hyaluronic acid, suddenly developed a white skin around the tip of his nose. The bridge of the nose was incredibly painful. Thanks to our training, the doctor was able to save the tissue by immediately injecting the right amount of hyaluronidase into the right place, thus controlling the situation to the patient's benefit.

CM: The filler antidote Hylase Dessau is being withdrawn from the market. What does this mean for aesthetic medicine?

S. Hilton: This is a disaster for all colleagues who treat with hyaluronic acid! Hylase Dessau was our safe anchor when unwanted results, or

more importantly vascular occlusion, occurred due to hyaluronic acid. There are currently no good alternatives to Hylase Dessau, because they are either not approved or significantly less effective or are associated with more severe side effects for patients. This presents the entire industry with a dilemma: can we continue to perform filler injections if we are unable to react adequately in an emergency? Hyaluronic acid has been the gold standard among fillers for 30 years due to the existence of an antidote. This would definitely change.

T. Fischer: It is irresponsible to leave doctors alone with this uncertainty. The industry must be held accountable. Hyaluronic acid should only be sold if the appropriate antidote is available. We should hold the industry responsible. Selling hyaluronic acid is a lucrative business, it must continue to be done responsibly and with accountability.

CM: What measures do you suggest to minimise the risk of vascular complications?

T. Fischer: We need a voluntary commitment from the companies selling hyaluronic acid to be able to supply hyaluronidase. At the same time, we need to provide better training for doctors. ISAC is currently working on an international standard for safety protocols.

S. Hilton: Patients also need to be better informed. Many are not even aware of how dangerous aesthetic treatments can be if they are not performed by experienced doctors



THE CHALLENGE OF HYLASE DESSAU

Background: Hylase Dessau has been on the market for 50 years and has a wide range of therapeutic uses. It is approved for extravasation and for better spreading of local anaesthetics. It has been an important drug in ophthalmology for over 50 years. However, it has an off-label indication for the dissolution of hyaluronic acid.

- **The problem:** Hylase Dessau, the drug used to treat vascular complications, will no longer be produced from 2025 (date not yet definitively set).
- **The alternatives:** There are currently products that are not approved in Germany and do not offer the same effectiveness and safety. Alternatives have to be ordered from abroad.
- **The consequences:** Increased risk for doctors and patients, especially in cases of vascular occlusion and the threat of blindness.
- **The proposal:** Voluntary commitment by manufacturers to sell hyaluronic acid only in combination with an approved antidote. Or maintain production of Hylase Dessau.

who must be able to treat all side effects of their injections adequately and safely at any time, even those that are only theoretically possible, and thus spare the patient a great deal of suffering. Doctors need intensive training in both areas: injections and side effects.

Quote from an affected doctor:

'I never thought that I could endanger someone with an aesthetic treatment. But without the right antidote at hand, I would have felt helpless.'

CM: Dr. Fischer, how can the collaboration between the DGBT and ISAC help to improve patient safety internationally?

T. Fischer: The DGBT is a pioneer in training, while ISAC specialises in safety concepts and emergency management. Together, we can create international standards that give doctors more security and protect patients.

S. Hilton: Time is of the essence. We must act before more serious

complications occur. Our vision is an aesthetic medicine that not only guarantees beauty but also safety.'

Final word:

The future of aesthetic medicine depends not only on new technologies and products, but above all on the responsibility of doctors and manufacturers. Training and safety standards are the key – a responsibility that the DGBT and ISAC are tackling together.

Dr. Fischer, Dr. Hilton, thank you very much for the interview.



Interview with Arthur Swift on the Revanesse® product collection



Fig. 1: Dr. Arthur Swift, Plastic Surgeon.

Dr. Arthur Swift has been practicing the art of plastic surgery since 1984 and has served as the executive of several plastic surgical societies and international committees. In 2018 he founded Swift Beauty with the firm belief that knowledge is a powerful gift that needs to be shared. Swift Beauty has since evolved into an original series of live symposia, webinars, tutorials, podcasts and in-depth interviews with experts in the field of cosmetic enhancement. The result is a discerning curation of approaches, insights, tips and techniques that set an unprecedented standard of training for both novice and seasoned injectors. Publisher Douglas Grosse interviewed Dr. Swift when he was in Miami.

CM: As an experienced injector who has worked with all premium brands, why do Prollenium products belong to your favorites?

I have been an injector since the early 1990's. Back then, there were only two or three products. Nowadays there are many more. For me Prollenium offers a comprehensive product line in Canada, while in Europe and especially in Germany a selection of products such as Pure (non-cross-linked), Revise, KISS, Ultra, Contour, Outline and Shape is available. However, some products such as Sculptra have not yet been introduced in Europe. Revanesse® Revise is an outstanding product that was developed specifically for the tear trough. It was the result of a collaboration between Prollenium scientists and users like me who presented innovative techniques. With a modification rate of only 8%, Revanesse® Revise offers natural integration into the tissue and minimizes the risk of subsequent complications. The low modification makes the product more biocompatible and reduces possible immune reactions.

CM: Do you choose your filler based on the specific patient and treatment indication, or do you have a preferred product range?

I metaphorically describe fillers as 'house guests' because they remain in the body for a long time. The aim is to use products that integrate harmoniously into the body and do not cause any short-term or long-term problems.

Prollenium products are characterized by minimal modification and a proven high level of safety, which is supported by medical studies. That is why, I have been using Revanesse® and other Prollenium products for over 9 years in my clinic.

CM: When did you first start using Revanesse®, and what prompted you to try it?

I've used Prollenium products for around 15 years, when I met Ario Khoshbin (Founder and CEO) and his scientific team. The Prollenium products form the major backbone of my practices in Montreal, Los Angeles, Miami, and New York.

Prollenium employs advanced techniques like wet milling to hydrate the product before application, ensuring superior tissue integration.

The company uses minimally invasive modification methods to preserve the natural structure of the hyaluronic acid. This increases biocompatibility and reduces the risk of swelling or inflammation. Particularly noteworthy is the uniform particle size of Prollenium products, which is achieved by using the most advanced sieving and dialysis processes.

CM: What sets Revanesse apart from other products on the market?

Although all hyaluronic acid products start with the same raw materials, the manufacturing processes vary considerably. Prollenium stands out due to the use

of uniformly round particles that cause less irritation. These particles reduce the likelihood of bio-film-associated reactions, which are often identified as the cause of subsequent inflammatory complications.

Careful control of pH, lidocaine addition, and purity during manufacturing ensures that the products are safe and effective. The science behind these processes helps to minimize the risks of immune reactions while ensuring natural results.

CM: In your opinion, what makes Revanesse a next generation/ different HA filler?

Revanesse® stands out due to its Thixofix cross-linking technology, which simplifies the injection process and enhances the product's natural feel and moldability. This technology minimizes swelling and inflammation because the hyaluronic acid molecules are smaller and more uniform. Many fillers use BDDE for cross-linking, but Prolenium's unique stabilization method ensures better biocompatibility. This results in a product that's more readily accepted by the body and offers a smoother, more natural application.

CM: Do you have a favorite product within the Revanesse® range, and if so, why?

One of my favorite products is Revanesse® Revise, which I developed together with the scientists of Prolenium and which gives great results especially in the tear trough area. Ultra is probably the one that's used the most because it's sort of an intermediate grade product, when it comes to viscosity. I also believe in cohesivity, and I think it works well with a lot of different areas, which is why it was probably called Revanesse® Versa in the United States, because it's so versatile.

For contouring of the chin or the jawline, I jump to Revanesse® Shape. Shape is a more robust product. Because what you do is, you kind of marry the product to the anatomy of the region. So, if it's a patient that has very thick sebaceous skin, or is Asian Afro American or has other ethnic reasons to have thicker skin I want to use a more robust product, I use Revanesse® Shape.

CM: How do you envision the future of the filler/injectable market? What innovations or advancements do you think are on the horizon?

The future of aesthetic medicine lies in hybrid fillers that combine the advantages of hyaluronic acid and collagen stimulators such as PLLA. Prolenium is working on a product called Revanesse® Matrice, which is expected to be launched in Europe by 2025/2026.

The combination of these technologies not only enables immediate results through volume build-up, but also long-term effects through collagen stimulation. Developments similar to Allergan's HarmonyCa product show that the market is trending towards multifunctional fillers.

Prolenium products offer a superior choice for physicians and patients thanks to innovative technologies, minimal modification and the highest safety standards. Their versatility, natural results and innovative approaches such as adhesiveness make them a forward-looking option in aesthetic medicine. With the ongoing development of hybrid fillers and new technologies such as Matrice, Prolenium remains at the forefront of the industry.

Dr. Swift, thank you for the interview.



**Svetlana Michels,
Director Injectables DACH**

ALMA TAKES OVER THE DISTRIBUTION OF REVANESSE IN THE DACH REGION

Alma is pleased to take over the exclusive distribution of Revanesse in the DACH region. Together with our strong partner Prolenium, we are setting new standards in aesthetic medicine. With Revanesse, we offer physicians an innovative product that combines maximum safety, excellent results and maximum patient comfort - the perfect addition to our Alma portfolio. Our team is full of enthusiasm and ready to embark on this exciting journey. Together we are shaping the future of aesthetics.

We look forward to sharing this vision with you!

Global Consensus for the Management of Acute Complications from Hyaluronic Acid Injections in Aesthetic Medicine

TANJA FISCHER¹, PIERRE ANDRE, OFIR ARTZI, BEATRIZ BELTRAN, SU BECKER-WEIMANN, HAGAI BETZER, HUGUES CARTIER, OLIVIER CLAUDE, IÑIGO DE FELIPE, TOM DECATES, RONALD FEINER, GREG GOODMAN, LISA GRUNEBAUM, JONATHAN KADOUC, SAAMI KHALIFIAN, WENDY LEE, STEVEN LIEW, LEONARDO MARINI, JOHN MARTIN, BEATRIZ MOLINA, RACHNA MURTHY, JAMES NEFFENDORF, HA NGUYEN HONG, ALEXANDRA OGILVIE, TAPAN PATEL, ERIC PETZOLD, THOMAS RAPPL, WOLFGANG REDKA-SWOBODA, HERVÉ RASPALDO, ALEXANDER RIVKIN, KELSEY ROELOFS, JONATHAN ROOS, CHRISTOPHER ROWLAND PAYNE, LEONIE SCHELKE, TODD SCHLESINGER, ROBYN SIPERSTEIN, PHILIPPE SNOZZI, NENAD STANKOVIC, ZIAH TAUFIG, JESPER THULESEN, PATRICK TREACY, JANI VAN LOGHEM, JOAN VANDEPUTTE, PETER VELTHUIS, INES VERNER, ANDRE VIEIRA BRAZ, SIMONE VOGEL, HEIDI A WALDORF, STEVEN WEINER, SANDY ZHANG-NUNES, THOMAS ZIMMERMANN AND MARINA LANDAU²

The increasing popularity of hyaluronic acid (HA) injections in aesthetic medicine is associated with rising numbers of cases of rare but serious vascular complications such as ischemia, necrosis, scarring, and blindness. These events, primarily caused by arterial occlusion from embolism, spasm, or compression, require swift and effective management. Recognizing the critical need for standardized intervention protocols, the ISAC World Board, consisting of 55 physicians from 23 countries, conducted an international survey addressing 20 key questions regarding acute complication management. The results revealed an extraordinary consensus, with several points achieving 100% agreement, enabling the development of an evidence-based, step-by-step algorithm for first-line treatment.

This protocol has been integrated into training programs worldwide,

serving as the foundation for national and international guidelines. For instance, Germany has introduced a comprehensive 'I-Secure Emergency Course' to equip practitioners with the skills to manage such complications effectively. Adhering to these standardized protocols not only improves patient safety but also provides legal protection for practitioners. Furthermore, thorough patient education, including the use of emergency interventions such as hyaluronidase (Hylase), remains vital.

The ISAC consensus and its algorithm represent a global safety standard in aesthetic medicine. They provide a foundational framework for the creation of national guidelines, ensuring consistency and reliability in managing complications across diverse healthcare settings.

LACK OF CLINICAL DATA

The occurrence of side effects following HA injections to the face has been documented in case reports or small series of case studies, which have been summarized in systematic reviews or meta-analyses [1].

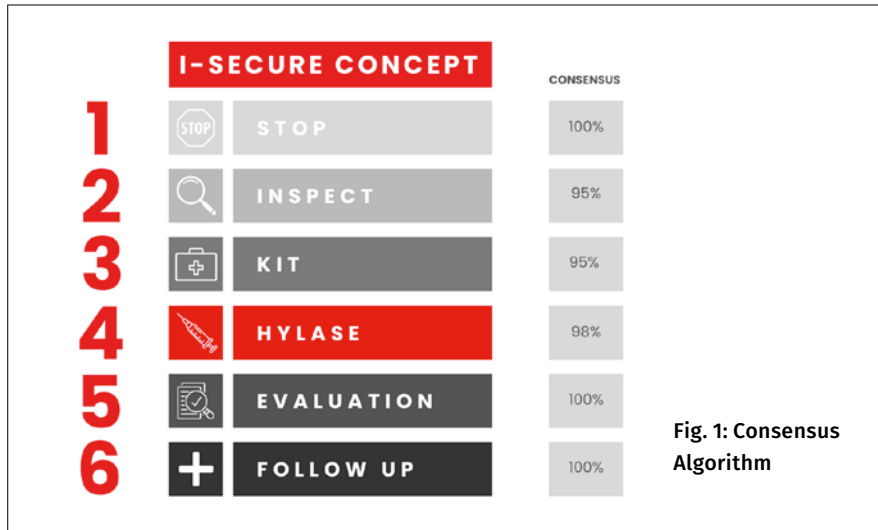
Taken together, the available data are still very poor. When it comes to the treatment side of side effects, the available data are even sparser [2]. Recommendations for treatments for severe side effects are largely based on single or few authors best practice recommendations [3–6]. Although we cannot provide new datasets for the treatment of severe vascular side effects, we have attempted to provide better guidelines by broadening the expert panel to a substantial number of internationally active experts in the field.

CONSENSUS ALGORITHM AND NATIONAL GUIDELINES

The consensus protocol established by the ISAC World Board serves as the foundation for training and national guidelines worldwide. For example, Germany has developed dedicated guidelines for the recognition and management of HA-related complications, incorporating the ISAC algorithm. Training programs such as the 'Secure Emergency Course' in Germany have been designed to teach practitioners how to apply these protocols effectively.

1 Dermatology and Laser Centre, Potsdam-Berlin, Germany,

2 Shamir Medical Center, Herzliya, Israel, all other affiliations see online publication



The algorithm (Fig. 1) was developed from the items with the highest consent (>94%) and provides a step-by-step approach for the acute management of complications:

1. Stop the injection immediately.
2. Analyze the skin for signs of ischemia: paleness, pain, or specific patterns of discoloration.
3. Involve the medical team and initiate therapy with hyaluronidase (Hylase) to dissolve the filler causing the blockage.
4. Monitor the time and consider repeated injections of hyaluronidase as needed until circulation normalizes.
5. Apply heat (warm compresses) and perform a gentle massage to improve blood flow in the affected area.
6. Discharge the patient only when the symptoms have improved and the patient is stable. Schedule a follow-up the next day.

If necessary, implement additional therapies such as antiseptic creams, corticosteroids, pain relief, aspirin (ASA), or vasodilatory substances, hyperbaric chamber. For other issues, e.g. 'Time to inform about off-label use of hyaluronidase' or

'Use of ultrasound during hyaluronidase injection' the answers were less unequivocal and not included in the guideline.

LEGAL AND EDUCATIONAL IMPLICATIONS

Standardized protocols also play a crucial role in legal protection for practitioners. Adherence to evidence-based algorithms provides a defensible position in medico-legal cases, emphasizing the importance of documented protocols in protecting both patients and physicians. Furthermore, patient education is critical, including thorough discussions of potential adverse events and the role of emergency interventions such as hyaluronidase (Hylase) in dissolving filler material.

CONCLUSION

The ISAC World Board's consensus represents a landmark achievement in the global effort to ensure safety in aesthetic medicine. By creating a step-by-step algorithm for managing complications and serving as the basis for national guidelines, this initiative addresses a critical gap in practitioner preparedness and patient safety. As the aesthetic medicine market continues to grow,

these protocols provide a much-needed framework for effective and consistent management of complications, fostering confidence and safety in the field. Future studies using large datasets of cases or controlled clinical studies are required to substantiate these best practice recommendations by clinical evidence.

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2025 AAD ANNUAL MEETING

March 7–11, Orlando, FL, USA

Further Information:
www.aad.org

AMWC MONACO 2025

March 27–29, Monaco

Further Information:
www.amwc-conference.com

11TH WORLD CONGRESS OF MELANOMA IN CONJUNCTION WITH THE 21ST EADO CONGRESS

April 3–5, Athens, Greece

Further Information:
<https://worldmelanoma2025.com>

32ND STUTTGART ADVANCED COURSE FOR RHINOPLASTY

April 9–11, Stuttgart, Germany

Further Information:
<https://stuttgart-rhinoplasty.com/>

DUBAI DERMA 2025

April 14–16, Dubai, UAE

Further Information:
<https://dubaiderma.com>

COMBINED OTOLARYNGOLOGY SPRING MEETING (COSM)

May 14–18, New Orleans, LA, USA

Further Information:
<https://cosm.md>

EADV SYMPOSIUM 2025

May 22–24, Prague, Czechia

Further Information:
www.eadv.org

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 Neuromodulator
 Guide 2025

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 Wound treatment:
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 new developments

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 Behçet's disease –
 an update

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May 29–31, Las Vegas, NV, USA

Further Information:
www.vegascosmeticsurgery.com

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Further Information:
www.icd2025rome.org

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