



**A Prospective Multi Centre Clinical Study to
Evaluate the Safety And Effectiveness
of the Soft Filler amalian® SF 24 advanced.**



Hyaluronic Acid

A natural substance that occurs in tissues throughout the human body:

- in the body of a 70 kg human ca.15g of hyaluronic acid are found.

Larger amounts are found in the skin:

- Dermis: 0.5 mg/ml
- Epidermis: 2-4 mg/ml

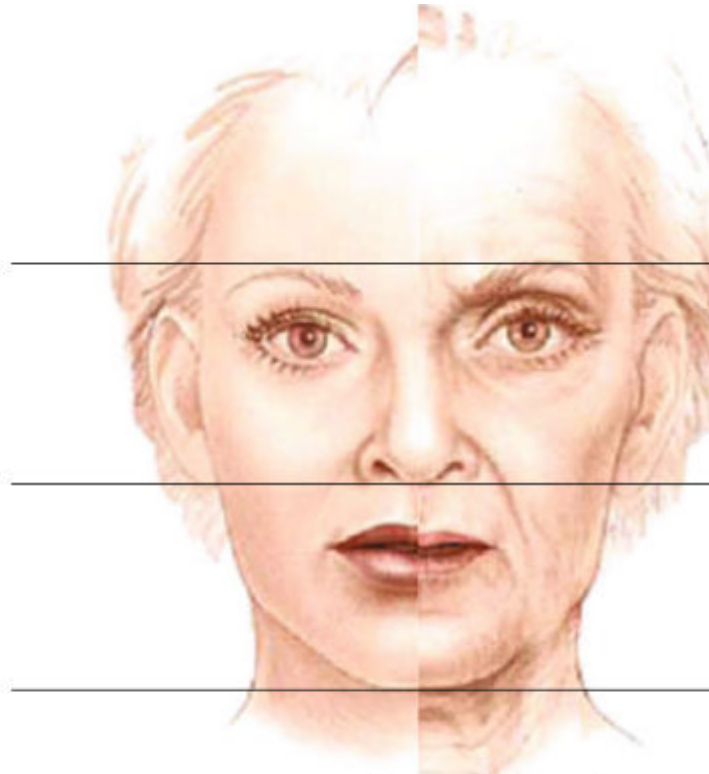
A non-toxic, non-immunogenic and biodegradable natural substance.

Hyaluronic acid is not only ubiquitous in human and animal tissue and is an **essential component** of the extracellular matrices in which most tissue differentiate.

Hyaluronic Acid and Aging

- Together with elastin and collagen hyaluronic acid gives structure and volume to the dermis.
- The content of hyaluronic acid in the skin decreases with age.
- Both intrinsic and extrinsic determinants modulate the rate and extent of skin aging i.e. loss of structural integrity and physiological function.
- The overall imbalance between biosynthesis and degradation of dermal tissue proteins, such as fibroblasts and glycosaminoglycans (most notably hyaluronan) , in the extracellular matrix, and the added strain of extrinsic factors leads to visible volume losses over time i.e. sagging, wrinkles and folds.

The Aging Face



Upper Third

- Weakened soft tissue structures
- Development of rhytides on forehead and glabella
- Brow ptosis
- Hollowing in temporal and infraorbital area

Middle Third

- Recession of soft tissue prominences near cheeks
- Loss of fullness in malar prominence
- Hollowing in buccal area, lower lids, and cheek
- Increased NLFs

Lower Third

- Thinning and laxity of skin
- Development of vertical lines above vermilion border of lip
- Loss of fat
- Development of jowls

Skin

- Dermal thickness ↑
- Loss of dermal turgidity
- Change in fiber architecture (Collagen ↓, elastin ↑)

Bone and Ligaments

- Volume ↓
- Glabellar/maxillary angle ↓
- Pyriform aperture ↑
- Rotation of craniofacial platform
- Elongation of orbitomalar ligament

Fat

- Volume ↓
- Atrophy
- Repositioning of compartments

Sadick NS et al, Aesthetic Plast Surg 2013 37:26-76

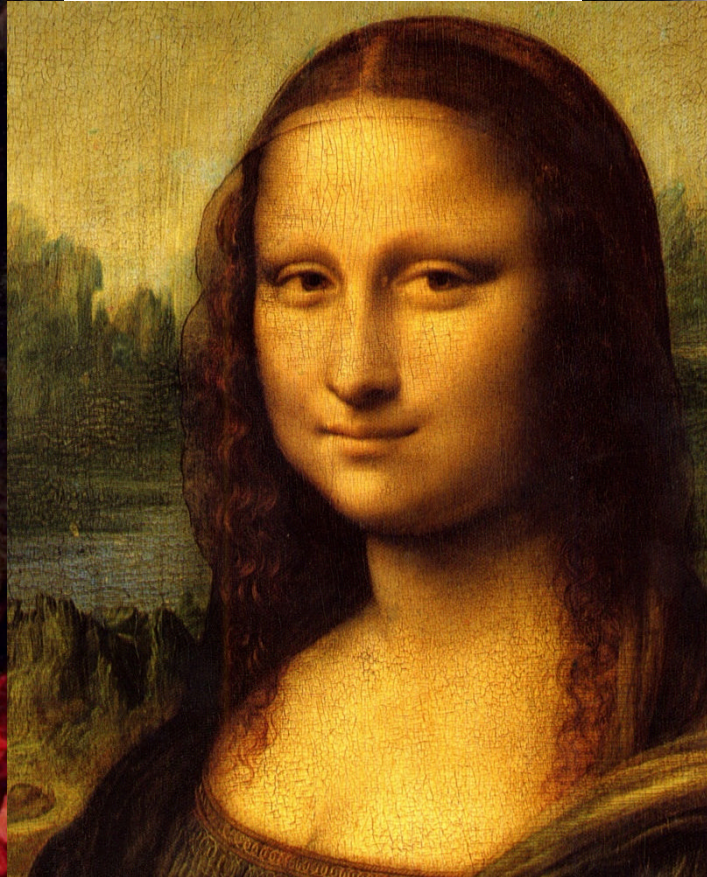
Synergistic effects of both intrinsic and extrinsic factors

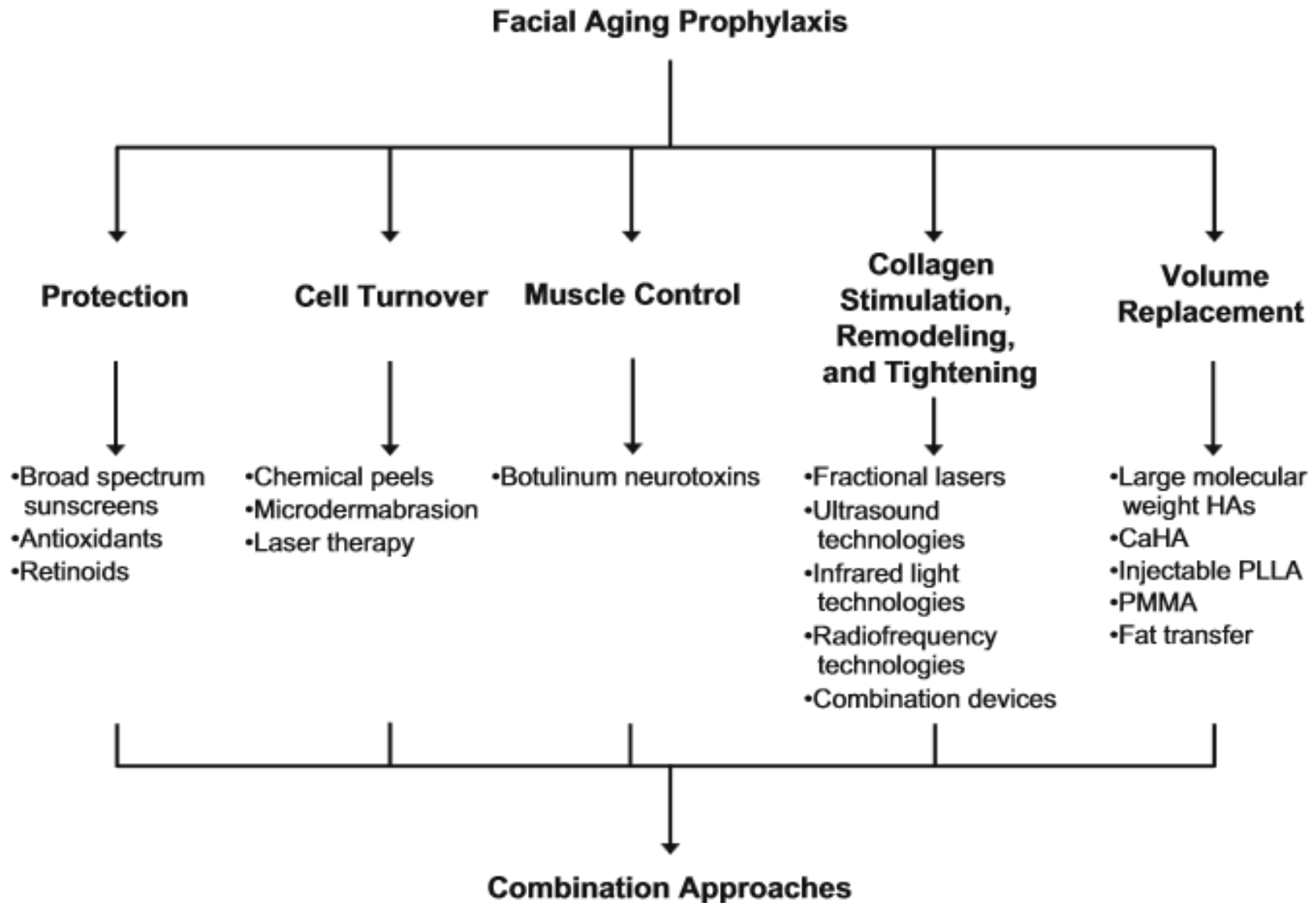
Intrinsic Signs of Aging	Extrinsic Signs of Aging	Physical Changes		Biochemical Changes
		Surface Changes	Colour Changes	
Epidermis thins	Epidermis thickens	Wrinkles Sagging or slack skin. Loss of firmness (tension). Thinner or thicker skin Loss of fat (accentuates wrinkles). Rough texture	Pigmentation Uneven tone Dull or lacklustre skin, Dilated capillaries (redness)	<ul style="list-style-type: none">• Loss of collagen and elastin production (skin loses tensile strength)• Loss of skin's ability to bind water (dehydrated skin)• Reduced/ loss of lipid production (skin becomes dry and skin barrier function is weakened)• Reduced blood flow (nutrients get delivered to cells less efficiently)• Reduced energy production (there is less energy for repairing DNA damage)• Slower cell turnover (skin cells take longer to shed and regenerate)• Impaired immune function• Formation of senescence cells (aging cells)
Fine wrinkles (after 60)	Coarse wrinkles (as early as 18), deep wrinkles, and furrowing			
Dermis and bones shrink (leads to sagging)	Dermis thins			
Fat decreases, especially fat pads above eyes and around mouth	Skin growths (actinic keratoses)			
Pigmented spots (lentigenes)	Mottled, uneven pigmentation			

Treatment with HA Fillers possible

Adapted from: <http://www.justaboutskin.com/anti-aging-skin-care-guide/skin-aging-overview/>

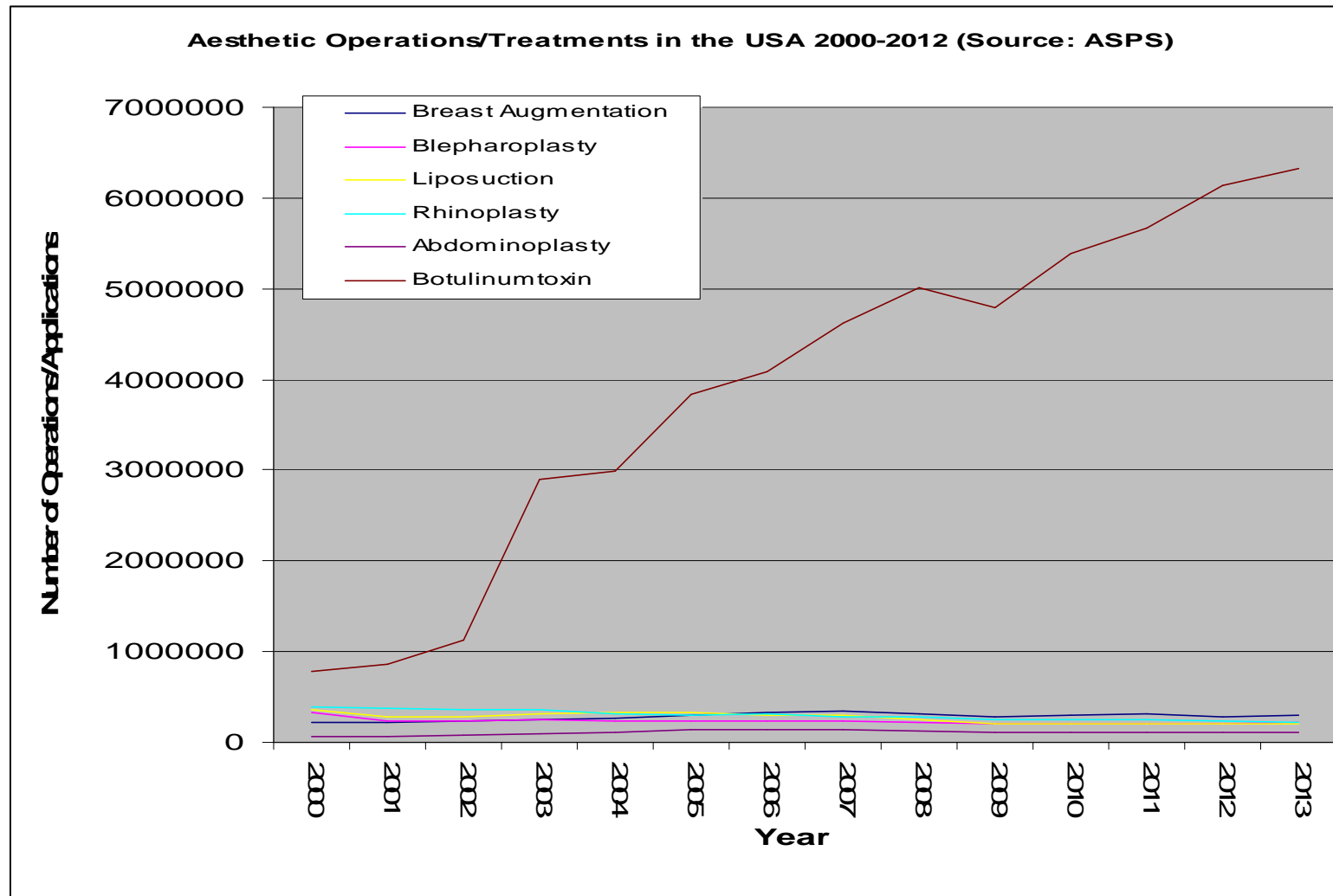
Definition of beauty



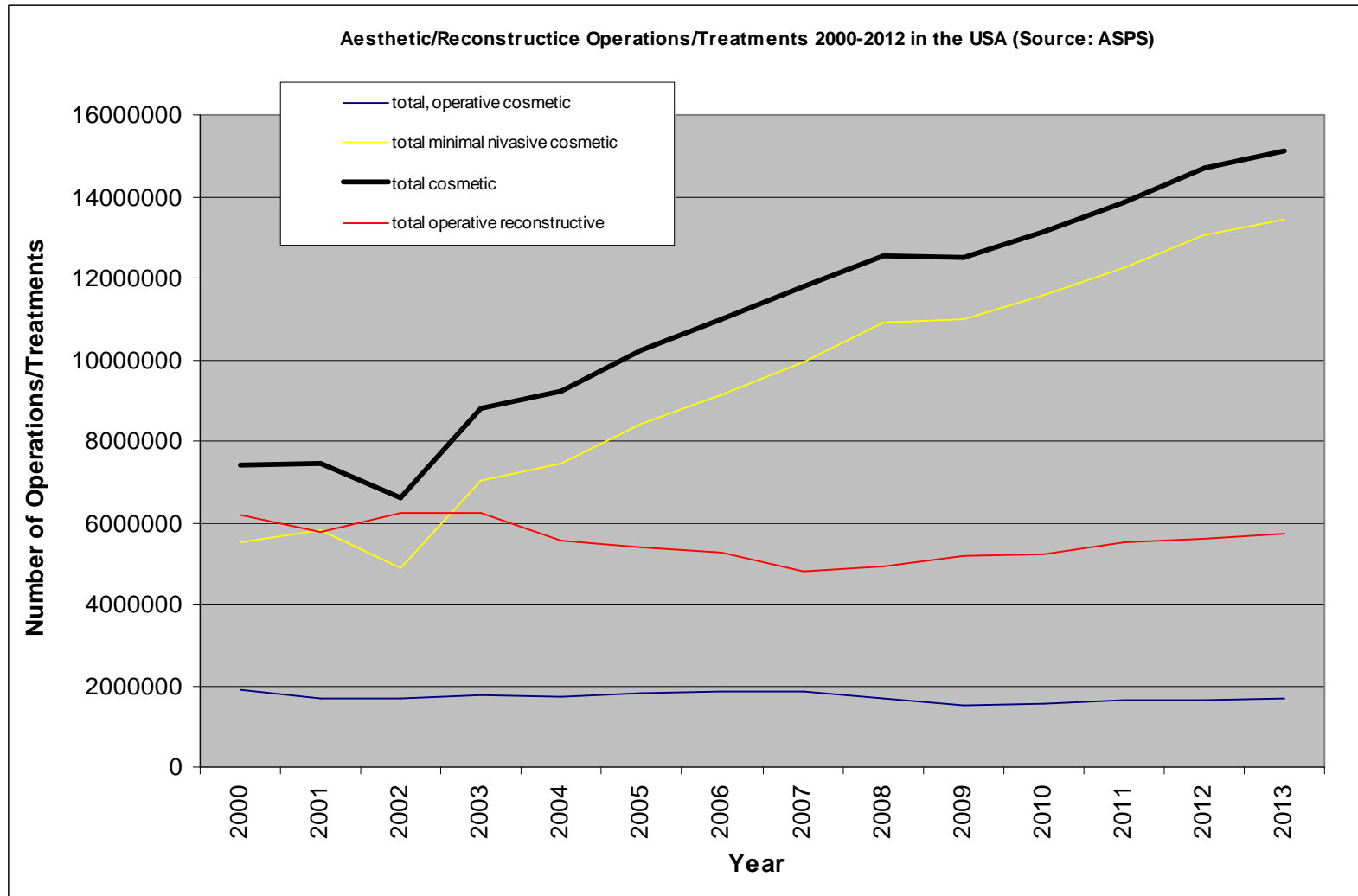


Sadick NS et al, Aesthetic Plast Surg 2013 37:26-76

Aesthetic surgery/ Treatments



Surgery versus Minimal invasive Treatments

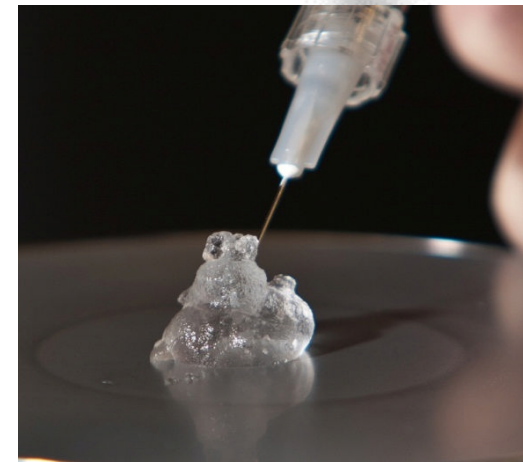


Hyaluronic Acid and Aging

- Hyaluronic acid fillers temporarily give back the lost hyaluronan and dermal volume, where by volume is restored (e.g. cheeks and lips augmented) folds are filled (e.g. NLFs) and wrinkles smoothed out (e.g. perioral wrinkles).
- Dermal fillers have been the most popular non-surgical procedure, treating various skin defects and volume losses, for five consecutive years in a row.

Hyaluronic Acid Dermal Fillers

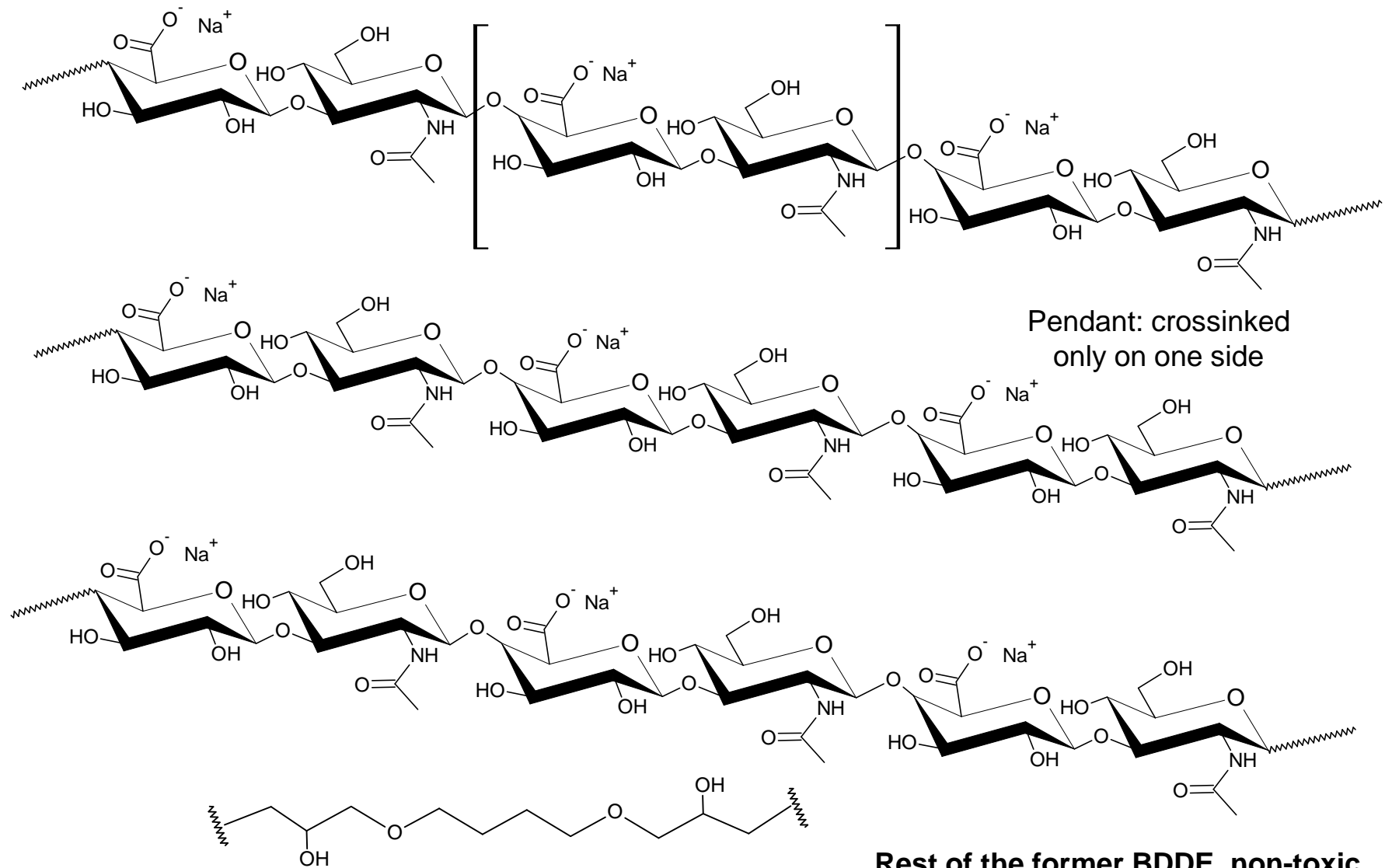
- HA a fairly simple structure, its solutions however show complex behaviour, delivering it's unique structural, rheological and biological properties
- This makes HA an excellent material for medical applications



Hyaluronic Acid Dermal Fillers

- HA has an exceptional water binding capacity (1 g HA can bind up to 1000 ml of water)
- Low to no allergic, immunologic or foreign body reactions and high biocompatibility
- HA gels are viscoelastic and pseudoplastic (reduction of viscosity under a shear force)
- Modification of HA delivers numerous forms of medical applications as: Nanocarriers, Micelles, stabilized tissue fillers, Hydrogels, Powders/mini-pellets, Implants, Sponges, Films, Conjugates

Hyaluronic Acid Dermal Fillers



Hyaluronic Acid Dermal Fillers

Cross-Linking

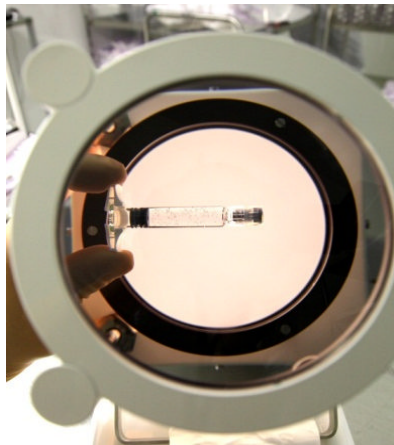
- „stabilization“ improves resistance to enzymatic degradation
- Achieves a complex chemical structure
- more robust physical barrier to the enzymatic and free radical breakdown in the phagocytes (Fredrickson 2008)

Hyaluronic Acid amalian® Dermal Implants

Hyaluronic Acid Dermal Fillers (Amalian®)

S&V's Dermal Implants are manufactured in **Germany** in every stage:

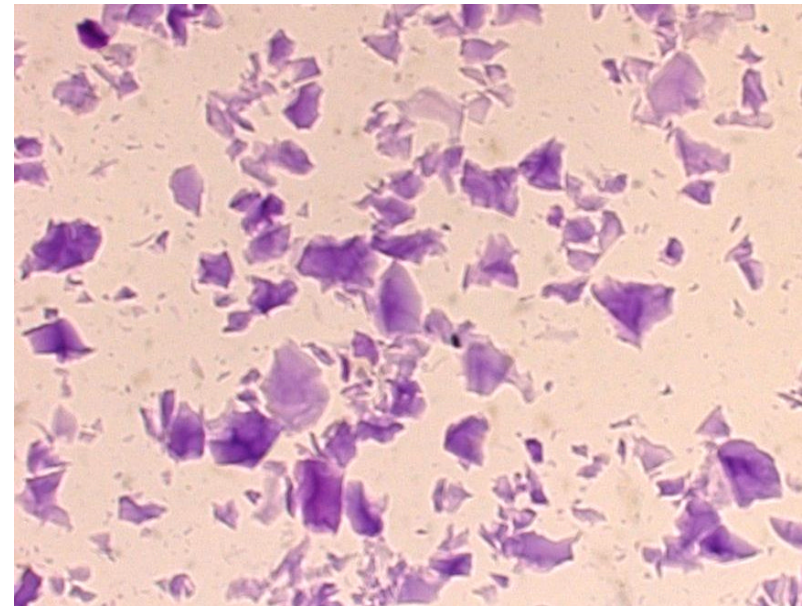
- from raw material acquisition, **cross-linking of the HA up to the final stages of filling**, packaging and labelling of each Dermal Implant; **including all of the quality control.**



Facility and Device: CE & ISO 13845:2016 certified

Hyaluronic Acid amalian® Dermal Implants

- First S&V dermal filler, developed in 2001 is a biphasic, highly cross-linked Hyaluronan gel available in two HA concentrations:
- 8.4mg/ml – 24mg/ml:
- **amalian® “Experts”**



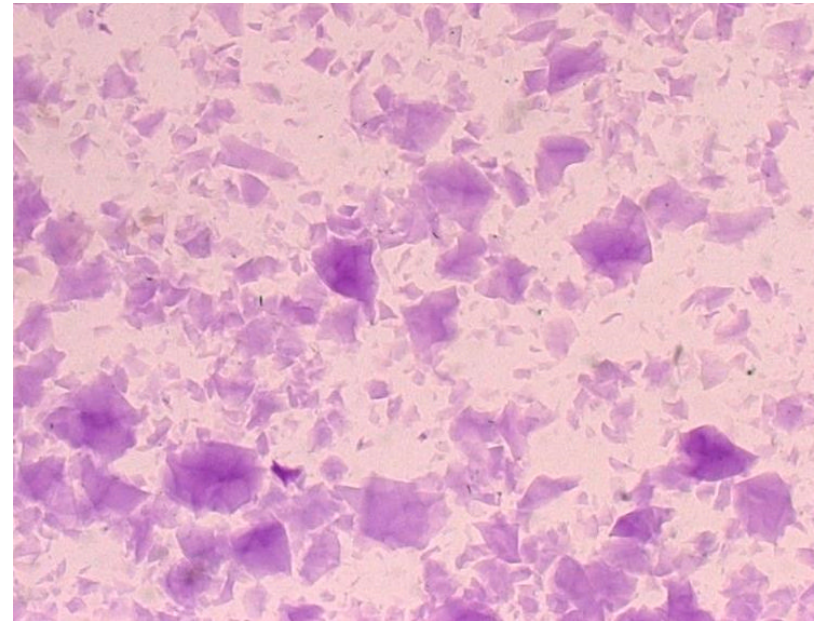
Hyaluronic Acid amalian® Dermal Implants

- Simultaneously, a linear non-crosslinked version was also developed for skin re-vitalisation and hydration i.e. mesotherapy:

amalian® “balance”

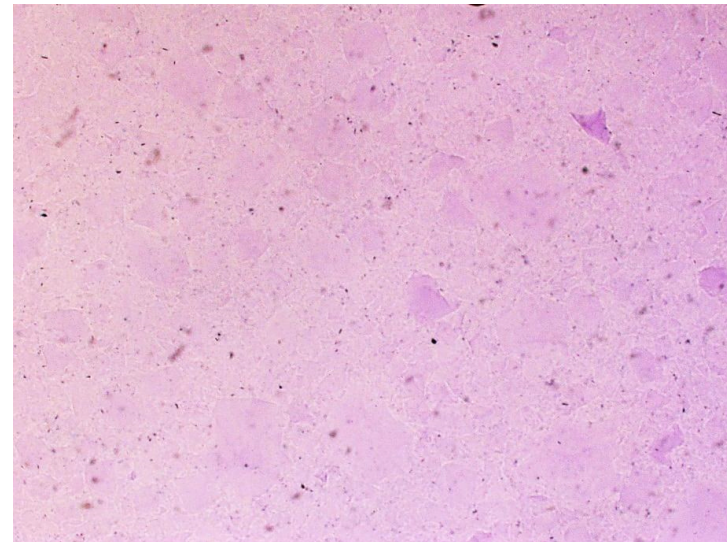
Hyaluronic Acid amalian® Dermal Implants

- Second S&V dermal filler product line, developed in 2011 is a monophasic low cross-linked Hyaluronan gel in four HA concentrations between:
 - 8.4mg/ml – 24mg/ml
- **amalian® “LT”**



Hyaluronic Acid amalian® Dermal Implants

- Newest dermal filler product line, developed in 2012 is also a monophasic cross-linked Hyaluronan gel in four HA concentrations between:
- 14mg/ml – 24mg/ml
- **amalian® “SF”**



Hyaluronic Acid amalian® Dermal Implants

Four different concentrations offer the options of mild augmentation in fine wrinkles up to strong volume build-up, e.g. in the cheek area to achieve an optimal result.

- amalian® SF 16 fine
- amalian® SF 20 medium
- amalian® SF 24 advanced
- amalian® SF 14 natural lips

Depending on the concentration, the effect of the amalian SF products last for 6 months.

amalian® SF 24 advanced has clinically demonstrated a prolonged effectiveness for far more than 6 months...

Hyaluronic Acid amalian® Dermal Implants



amalian SF 24 advanced – 24mg/ml HA

Soft, non granulated gel with hydrated, “saturated” particles for great injection comfort as well as:

- reduced swelling
- no adverse effects
- no SAEs
- no late reaction such as granuloma, lumps or migrations

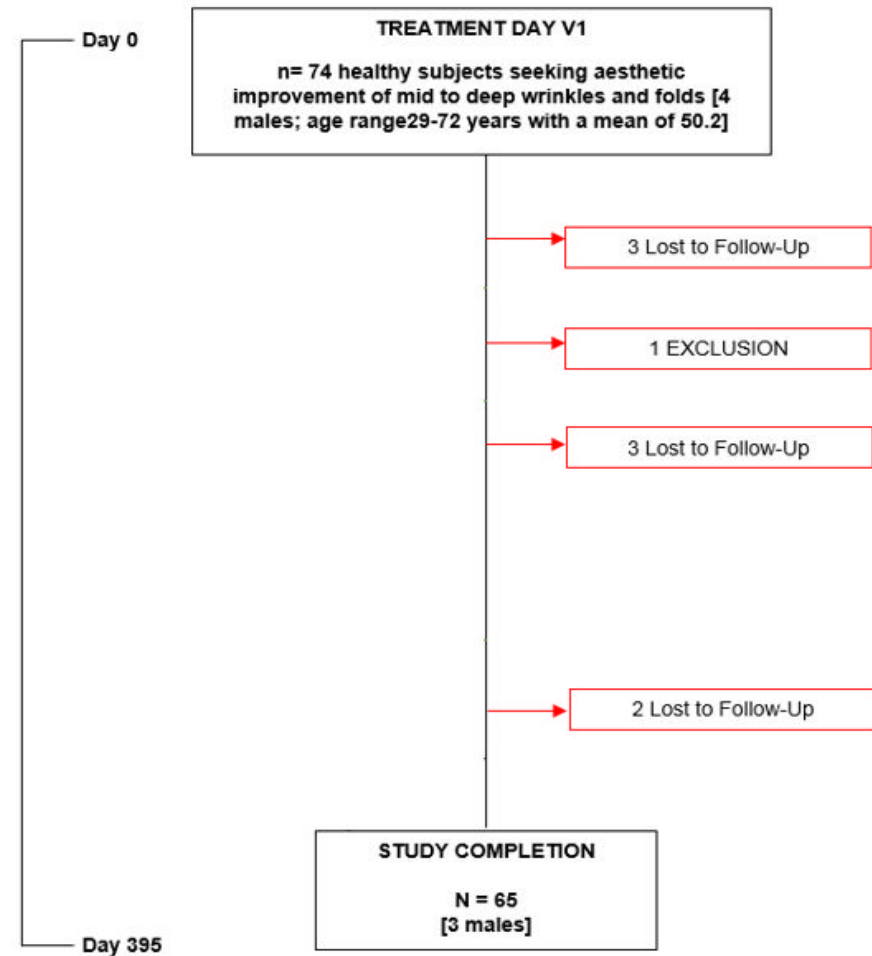
Whilst maintaining a long lasting effect of **9 months**.

amalian® SF 24 advanced – Clinical Study

- Study design: prospective, multicentre, post-market follow-up clinical study (PMFCS) - Open Label, No blinding
- Endpoint Classification: Safety and Effectiveness
- Conditions treated: volume losses/wrinkles or skin defects related to disease, age or injuries in facial soft tissue.
- Follow-up time: 395 days; visits after treatment at days 21, 121, 213 and 395.

amalian® SF 24 advanced – Clinical Study

- A total of 74 patients were enrolled across 5 centers in Germany.
- 8 were lost to follow up and one patient was excluded.
- N=65 completed the full follow up period (395 days).



amalian® SF 24 advanced – Clinical Study

Outcome Measures

Primary Outcome Measures	
Degree of Correction	Validated aesthetics scale (0 to 4) from no wrinkles to severe wrinkles/ sagging/folds.
Longevity	Duration of achieved correction in comparison to baseline values and degree of maintained correction.
Secondary Outcome Measures	
Responder Rates	Percentage of treated patients with at least +1 aesthetics scale point above base line value at each follow up visit.
Patient and physician satisfaction	Global Aesthetics Scale (GAIS) defining subjective assessment of worsening, unchanged, improved, highly improved and very highly Improved as: -1, 0, 1, 2 and 3, respectively.

amalian® SF 24 advanced – Clinical Study Outcome Measures

Details of Outcome Measures used
in Statistical Assessment

Effectiveness

Degree of correction	Aesthetics Scales	0	1	2	3	4
	Folds	No folds	Mild folds	Moderate folds	Sever folds	Very sever folds
	Lines	No lines	Mild lines	Moderate lines	Sever lines	Very sever lines
	Volume	Full	Mildly sunken	Moderately sunken	Severely sunken	Very severely sunken
	Contours	No sagging	Mild sagging	Moderate sagging	Severe sagging	Very severe sagging
	Wrinkles	No wrinkles	Mild wrinkles	Moderate wrinkles	Severe wrinkles	Very severe wrinkles
Longevity	Duration of achieved correction in comparison to baseline values [Aesthetics Scales] and degree of maintained correction at each follow-up visit.					
Responder Rates	Percentage of treated patients with at least +1 scale point [Aesthetics Scales] above base line value at each follow up visit.					
Patient and Physician satisfaction	Global Aesthetics Scale (GAIS) defining subjective assessment	-1	0	1	2	3
		Worse than before	Unchanged	Improved	Highly improved	Very highly improved
Safety						
Severity	4 point severity scale	0	1	2	3	4
		No reaction	Mild	Moderate	Strong	Very strong
Duration	In days from onset of event.					
Onset of event	After X days post treatment					
General AE/ SAE Reports	Free physician commentary/ site report					

amalian® SF 24 advanced – Clinical Study Treatment

Patients included in the study:

- healthy subjects over the age of 18 seeking aesthetic improvement for **volume loss and correction of mid to deep wrinkles** such as volume augmentation of cheeks, nasolabial folds and marionette lines.
- No touch-up treatments were allowed.
- Patients were not treated by any further fillers or nor did they receive other skin rejuvenation treatments in the whole follow-up period.

amalian® SF 24 advanced – Clinical Study Treatment

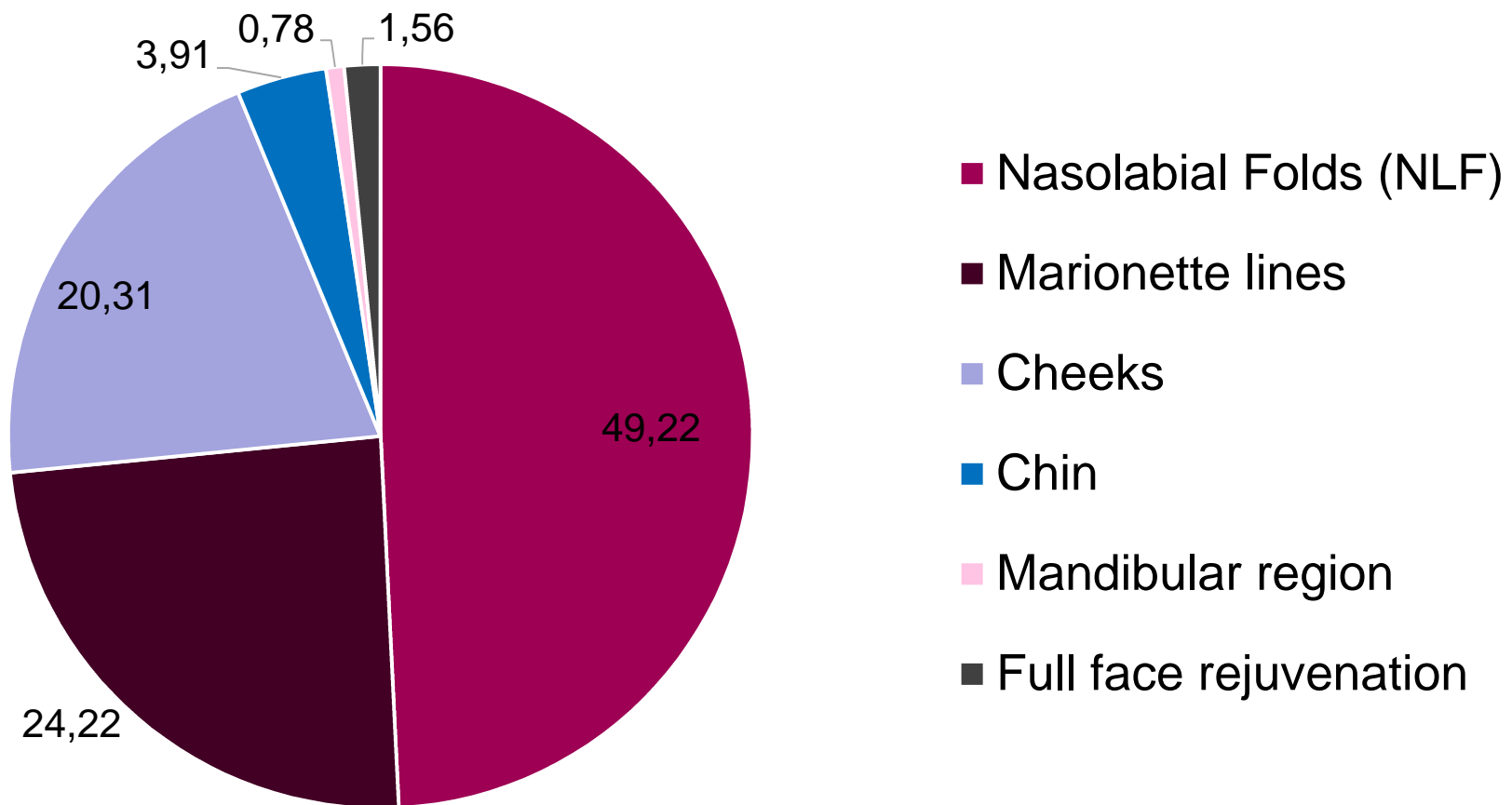
- Mean injected volume of 1.55 ml SF 24
- Maximum volume used to treat - 2 ml
- Minimum volume used to treat- 1ml

Application: with a 27G needle, into mid to-deep dermis

- A total of 128 areas were treated

Areas Treated	(%)
Nasolabial Folds (NLF)	49.2
Marionette lines	24.2
Cheeks	20.3
Chin	3.91
Mandibular Regions	0.79

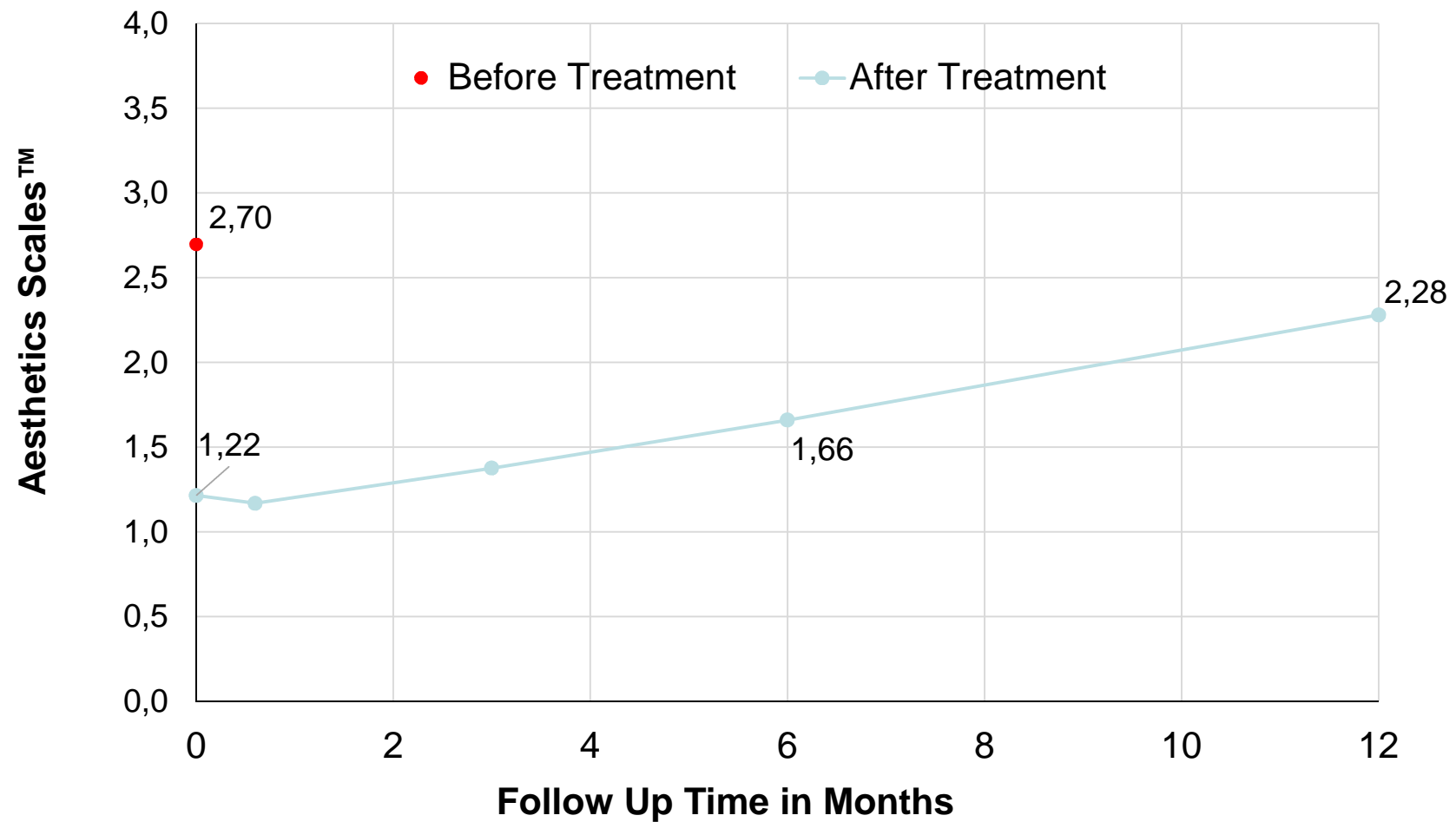
amalian® SF 24 advanced – Clinical Study Treatment



amalian® SF 24 advanced – Clinical Study Effectiveness

Achieved correction after treatment with
amalian® SF24 advanced

amalian® SF 24 advanced – Clinical Study Effectiveness



amalian® SF 24 advanced – Clinical Study Effectiveness

Baseline value = 2.7 was reduced to:

- 1.6 at day 213
- **1.6 at day 273 (9 Months)**
- 2.3 at day 395

Displaying significant improvement compared to baseline value (P value < 0.00001) of more than 1.0 scale points; even after 9 months.

amalian® SF 24 advanced – Clinical Study Effectiveness

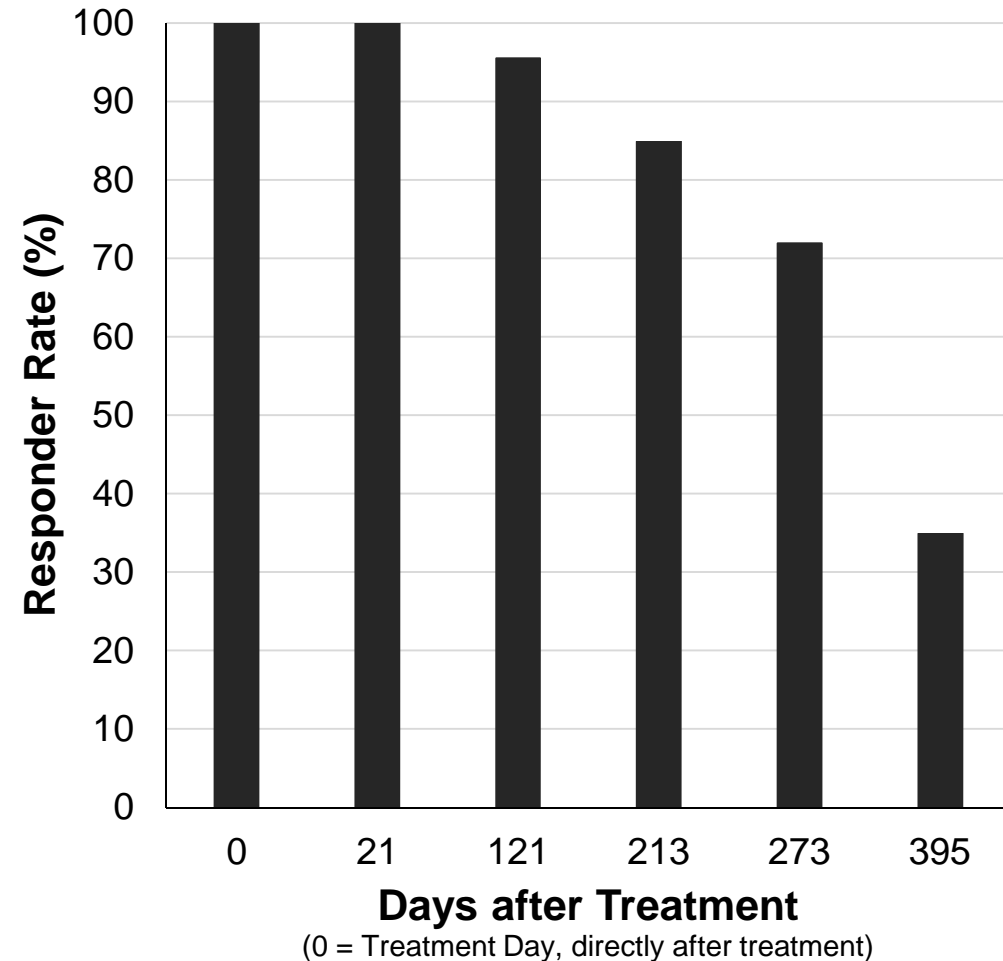
Responders = successful treatment when correction of ≥ 1 scale points to base line has been maintained

Product effectiveness is rated high when responder rates are $\geq 70\%$

amalian® SF 24 advanced – Clinical Study Effectiveness

Responder when:	Improvement of aesthetics scale points (Δ to baseline value) is:
Difference in Aesthetics Scales	≥ 1

Responder rates (%)	
Time after treatment in days	0
	100.00
	21
	100.00
	121
	95.45*
	213
	84.85*
	273
	71.88*
	395
	34.85





Before Treatment



Directly after treatment

Treatment of the NLF, Marionette Lines and sagging around the jawline with
0.5ml of amalian® SF 24 on each side

Frontal



Before Treatment



After 6 Months

Treatment of the NLF, Marionette Lines and sagging around the jawline with
0.5ml of amalian® SF 24 on each side

Side View



Before Treatment



Directly After Treatment



After 9 Months

Correction of uneven sagging of the jawline with 0.5ml
of amalian® SF 24 on each side

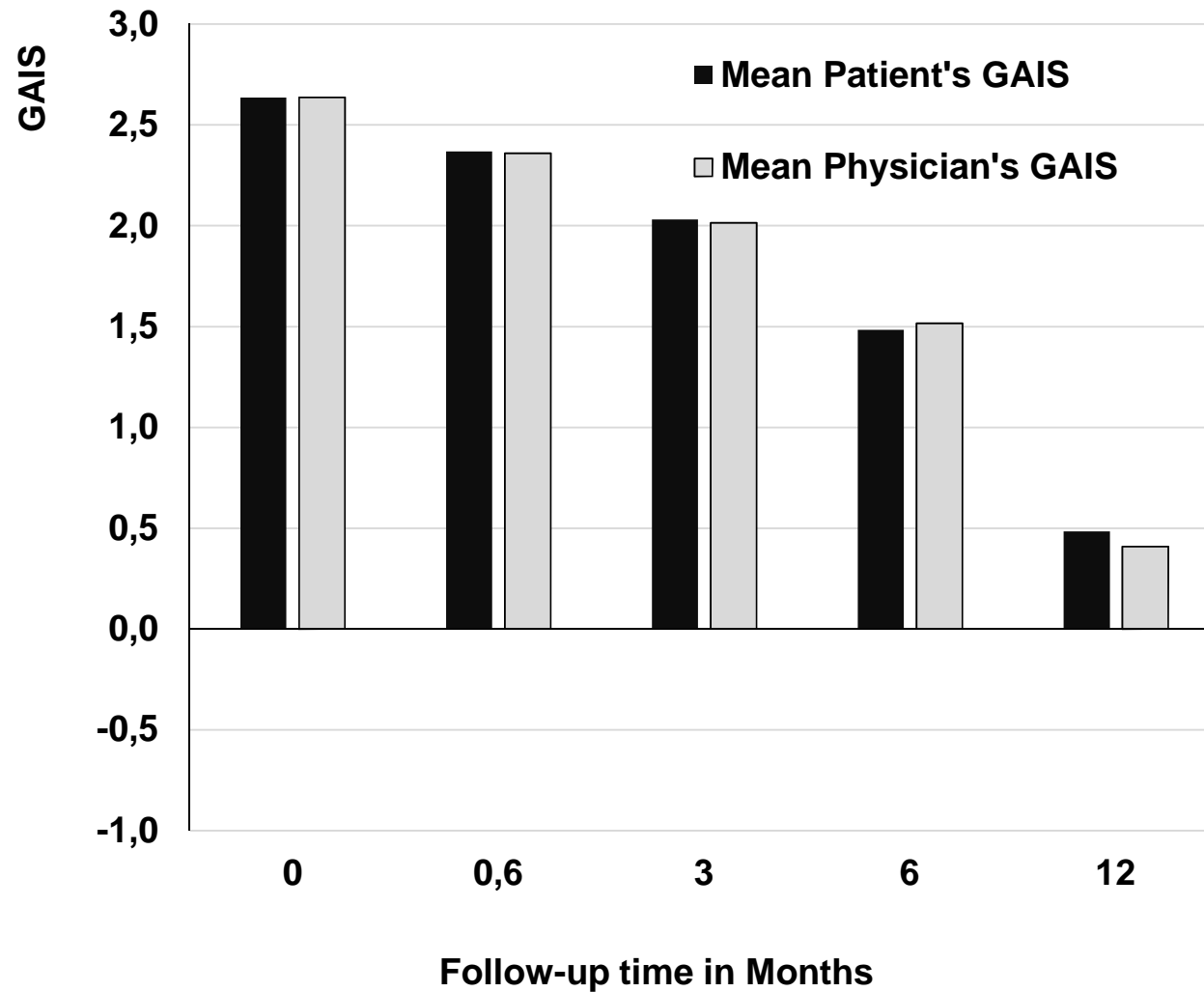
amalian® SF 24 advanced – Clinical Study Effectiveness

Patient and physician satisfaction (GAIS) remained high throughout the entire follow up period.

High satisfaction was not only due to effectiveness, but also due to:

- Safety
- Comfort during and after injection
- Ease of injection for the physician
- Ease of handling after injection
- Achievement of correction, whilst still maintaining a natural look

amalian® SF 24 advanced – Clinical Study Effectiveness



amalian® SF 24 advanced – Clinical Study Effectiveness

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- Achievement of correction, whilst still maintaining a natural look

amalian® SF 24 advanced – Clinical Study Safety

amalian® SF 24 advanced showed superior safety during treatment and the whole follow-up period.

amalian® SF 24 advanced – Clinical Study Safety

- No Adverse Reactions
- No SAE's
- No granulomas
- No nodules/ lumps
- No migrations/ dislocation
- No late on set reactions

amalian® SF 24 advanced – Clinical Study

Safety

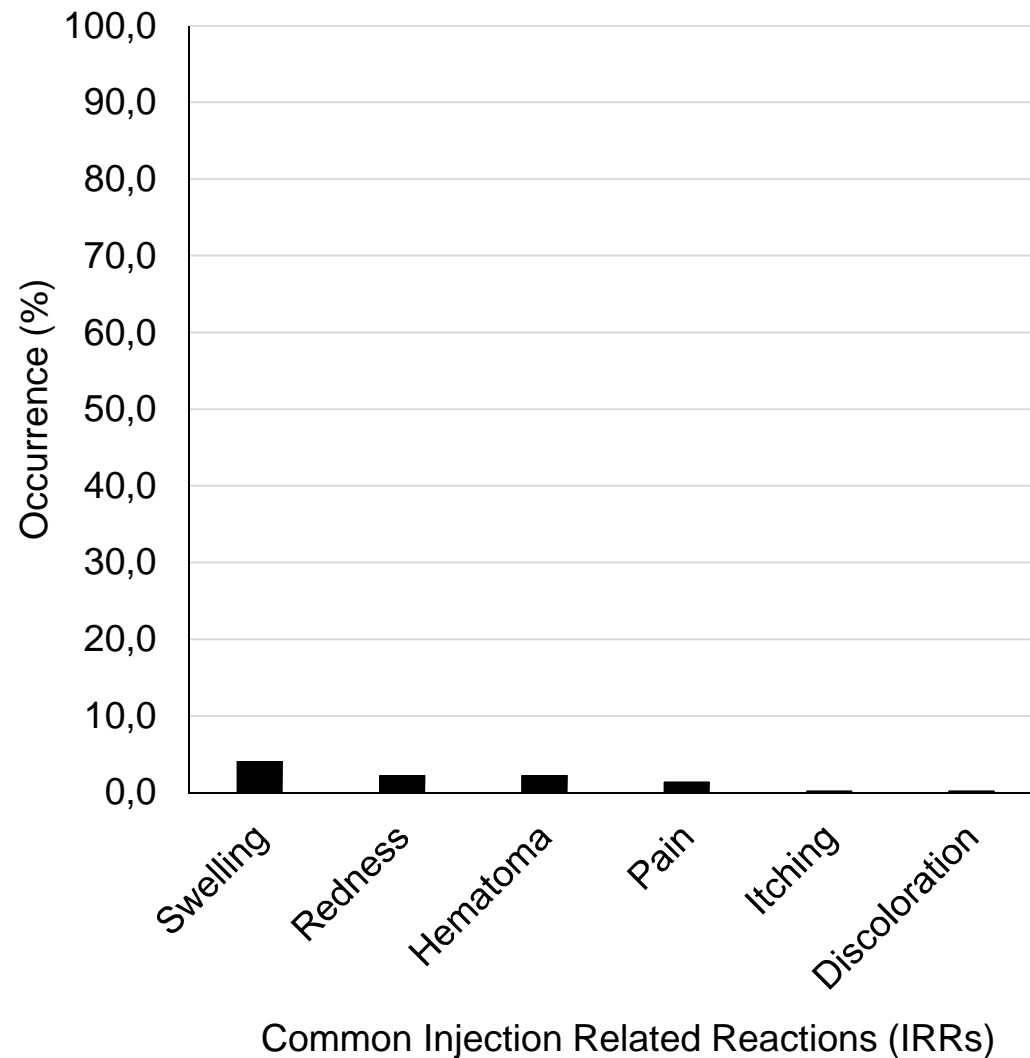
Injection related reactions (IRRs):

- swelling, redness, hematoma and pain with an occurrence rate of 4.04%, 2.19%, 2.19%, and 1.35%, respectively.

- Mean severity = slight & below moderate (≤ 1.5)

- Mean duration ≤ 72 hours

Isolated cases: itching and discoloration attributed to sensitivity toward topical anesthetic cream - (only in one patient)

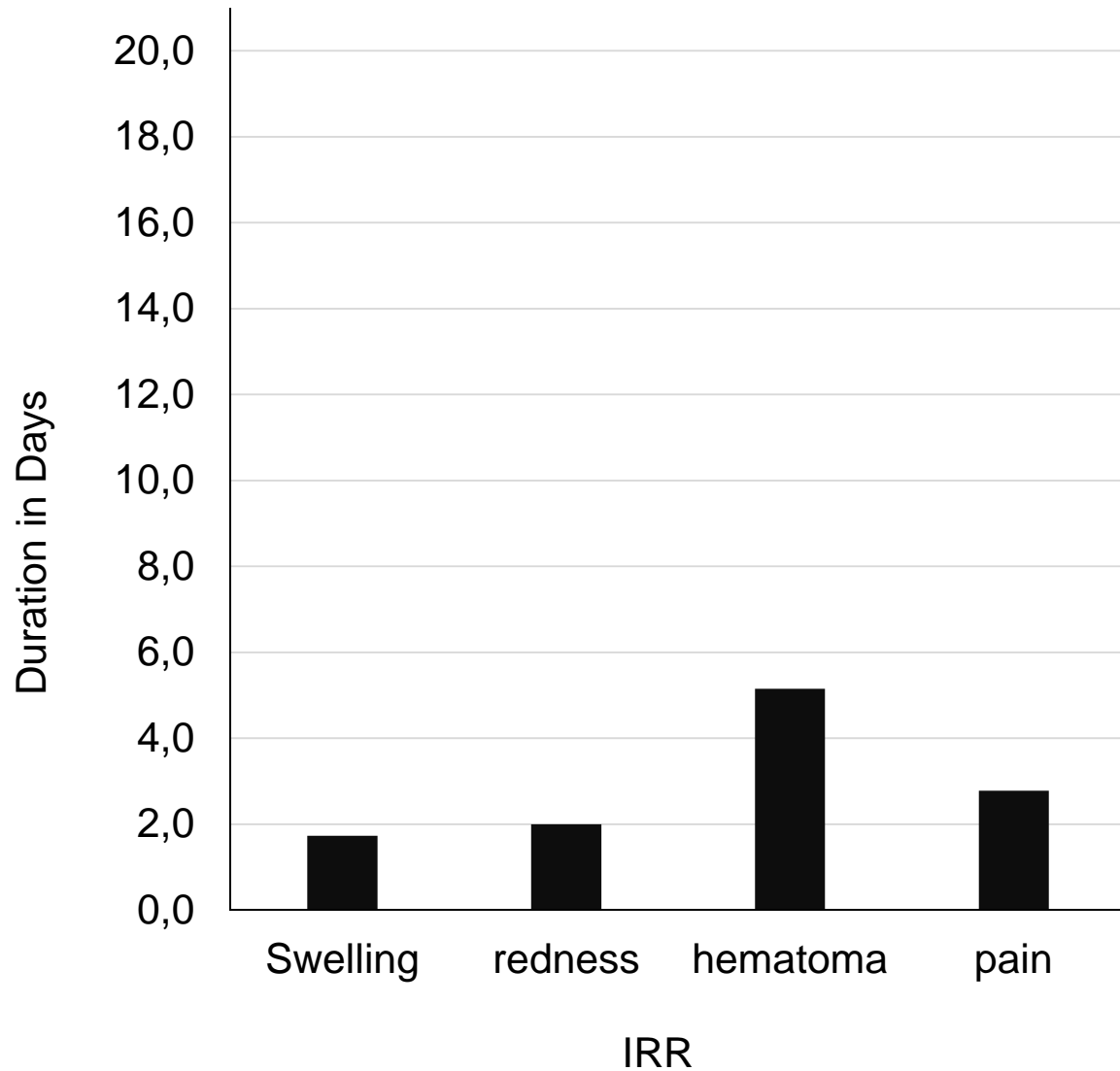


amalian® SF 24 advanced – Clinical Study

Safety

All IRRs were

- short-term (1 – 7 days);
 - mild to moderate in severity (1 -2)
- and
- resolved without intervention.



amalian® SF 24 advanced – Clinical Study Discussion

- Achieved improvement in correcting deep wrinkles and folds paired with the absence of adverse reactions, SAEs, prolonged or late onset side effects, delivers an ideal filler material (1) for patients seeking immediate correction, whilst expecting treatment comfort, safety and minimal down-time.

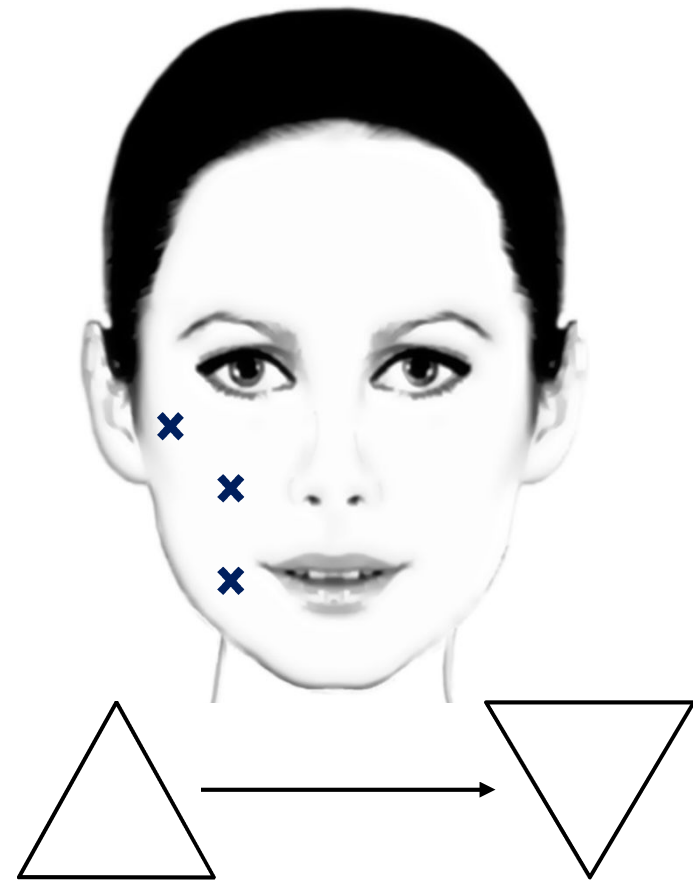
1. Gold M. H. Use of hyaluronic acid fillers for the treatment of the aging face. Clin Interv Aging. 2007;2(3):369-76.

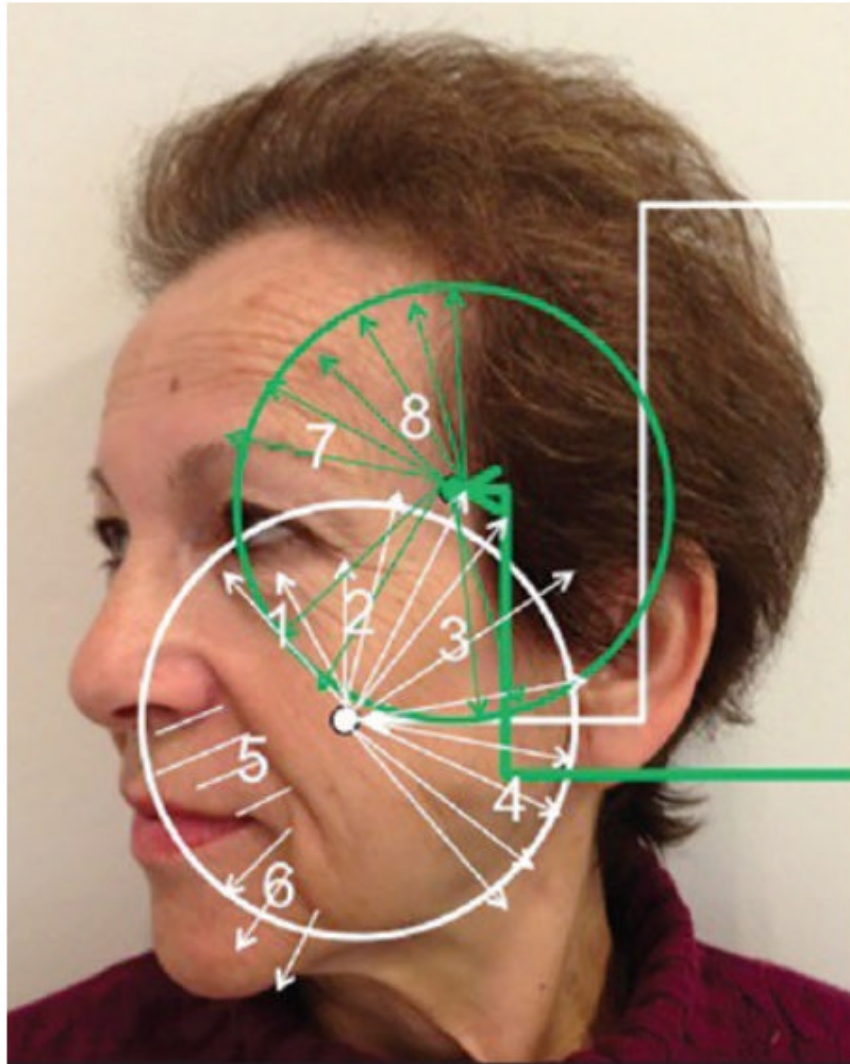
amalian® SF 24 advanced – Clinical Study Treatment

amalian® SF 24 advanced proved to be **an excellent choice for liquid lifting**

The technique of “Liquid Lifting” was deployed to treat patients seeking a general lifting and volume filling effect:

- Subtly lift drooping facial features like the brows and jowls
- Improves eye bags and sunken-ness under the eyes
- Lifts drooping corners of the mouth
- Corrects bumps on the nose





Points of entry:

A: mid cheek point.

B: Posterior fronto-temporal area.

I. d. Felipe and P. Redondo. The Liquid Lift: Looking Natural Without Lumps. J Cutan Aesthet Surg. 2015; 8(3): 134–138.

amalian® SF 24 advanced – Clinical Study Discussion

- The high content of HA in the device, compared to most fillers on the market, is a unique formulation providing long-lasting efficacy as well as superior safety - short and long term.
- The higher HA concentration (1) allows to fill and maintain a larger volume for a longer period, making this product most adequate for deep wrinkles, folds and volume augmentation.

1. Gold M. H. Use of hyaluronic acid fillers for the treatment of the aging face. Clin Interv Aging. 2007;2(3):369-76.

amalian® SF 24 advanced –For successful treatment

Adhere to the right plane

- Fillers for superficial injection placed too deep:
 - require larger volumes and longevity is reduced
- Fillers for deeper dermal layers injected too superficial:
 - result in lumps and blanching
- If lumping results mold filler immediately – max before 2 weeks after injection

amalian® SF 24 advanced – For successful treatment

Know the Anatomy

- Nasolabial folds display a degree of natural asymmetry – do not overcorrect, individualize
- Knowledge of facial vascular anatomy
 - Immediately stop the injection if a patient exhibits:
changes in vision,
signs of a stroke,
blanching of the skin,
unusual pain during or shortly after the procedure

amalian® SF 24 advanced – For successful treatment

Take Precaution Measures; Read the Instructions!

A main precaution measure is:

- careful investigation of the patient's history by the physician with respect to diseases, other anti-aging treatments and individual factors that may increase the risk of adverse reactions

ALSO

- Inject only into healthy, non-inflamed and disinfected areas of skin

Avoid overcorrection!!

Excessive hyaluronic acid gel implantation may result in formation of nodules, large swellings and dislocation.

amalian® SF 24 advanced – For successful treatment

“A comprehensive treatment plan should be devised to suit the needs of each patient. Choosing the right filler for the right indication is vital.”

M.Vedamurthy, A.Vedamurthy. Dermal Fillers: Tips to Achieve Successful Outcomes. J Cutan Aesthet Surg. 2008; 1(2): 64–67.

Conclusion

- HA fillers remain a safe and effective option
- SF 24mg/ml has been shown to bring long-lasting results
- Choosing the right material is important

