

KYSENSE®

Redefining the science and aesthetic of the facial
anatomy

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KYSENSE®

From Kylan, a Swiss company, with a large state of the art manufacturing facility in Casablanca, Morocco. Casablanca is the leading manufacturing, industrial and economic force in Morocco and is the country's principal port

Dell, IBM, Unilever, Procter & Gamble, Huawei, Nestle, Siemens (among others) have high tech manufacturing facilities in Casablanca

The famous Moroccan blue colour palette inspires our KYSENSE® branding with the deepest cobalt blue representing the deepest injectable SKU



KYSENSE®



KYSENSE®

KYSENSE®

KYSENSE® a sterile, transparent, resorbing gel of crosslinked sodium hyaluronate with undetectable BDDE

Without lidocaine means

- alerted to vascular occlusion earlier
- Minimised bruising
- Minimal swelling
- We aren't removing one of the signs of risk i.e. pain
- Patients can eat and drink post lip injection
- Lidocaine allergy
- Numbing cream is used for lip injections
- Deeper work and cannula use doesn't require lidocaine
- Minimising the risk of a negative interaction in the tissue

Engineered to be more comfortable to inject. Characteristics that make it more comfortable are

- Extrusion force no dilaceration on injection
- Ultra Sharp needles
- Smooth pharmaceutical grade hyaluronic acid
- 2.5million Dalton in molecular weight is anti inflammatory

CE MARKED under the MDR by notifying body 2797 BSI Group (Netherlands)

Demand for fillers grows year on year

HA filler global market to reach \$6.06 Billion by 2026

Europe (& UK) biggest market after North America

Ref: Acumen Research and Consulting

Key objectives in the development of KYSENSE®

- ✓ To provide a SAFE premium HA dermal filler as good as the market leading products
- ✓ To provide SUPPLE & FLEXIBLE crosslinked structure with a *low degree of modification on the market* to ensure a proper tissue distribution and integration and ability to move as one with the surrounding tissues
- ✓ To achieve HIGH VOLUMIZING filler with high PROJECTION POWER and HIGHER VISCOSITY with the correct rheological properties to lower migration risk
- ✓ To provide clinical natural results with high patient satisfaction over repeat treatments and to maintain NATURAL BEAUTY of the patient

KYLANE

An experienced team of Swiss dermatologists, plastic surgeons and scientists, recognised for their contribution to the market leaders in HA dermal fillers (Allergan, Merz, Vivacy, Croma)

The team regularly contribute to international peer reviewed publications in the field of tissue bio-integration of HA fillers and techniques in facial aesthetics

Set out to specifically to design the next advancement in filler technology – improved consistencies to allow natural outcomes, precise injections and durable projection capabilities

Achieved this with a reduction of BDDE (the crosslinking chemical process used in production of HA, crosslinking creates the firmness of the gel)

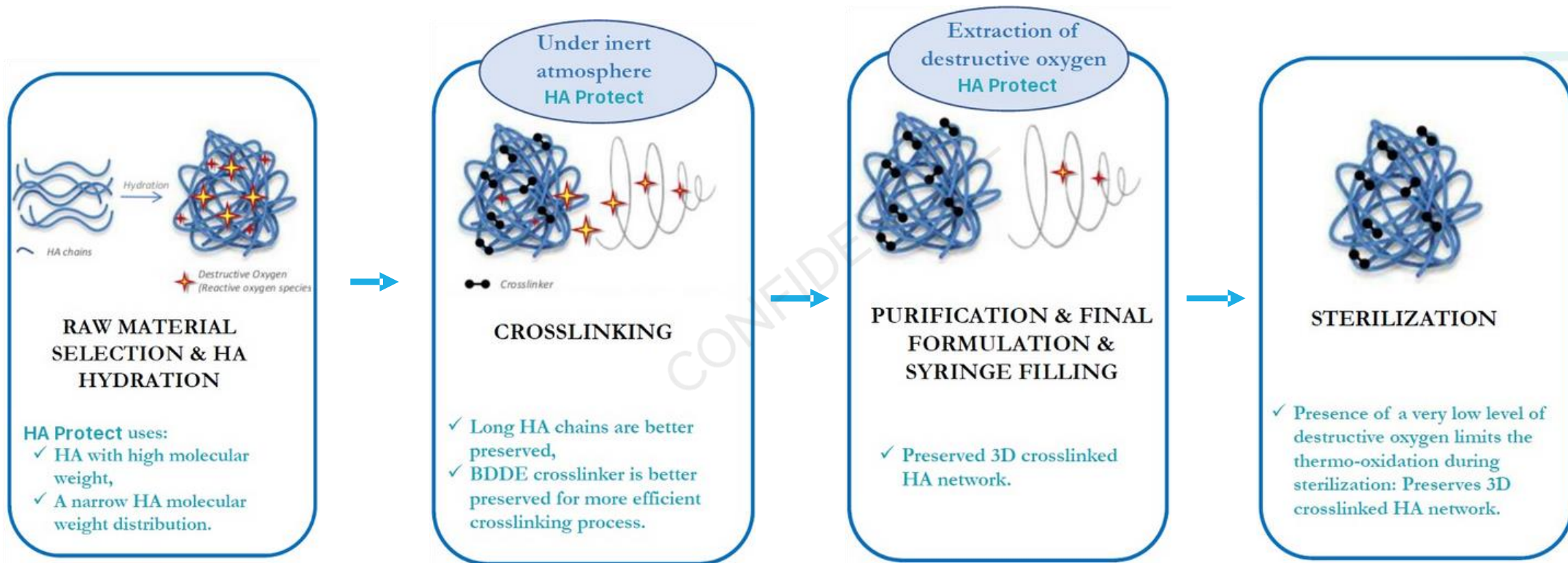
KYSENSE® is an advancement in the cross linking process to reduce the BDDE quantity to an almost undetectable level and therefore achieve a natural looking and feeling HA filler

How?

KYSENSE® is made using HA PROTECT technology which is the *extraction of destructive oxygen* during the manufacturing process, including during the crosslinking step.

KYSENSE® is manufactured in an inert oxygen free environment

This significantly PRESERVES the intrinsic properties of the HMW chains leading to a highly viscous and PROJECTING filler

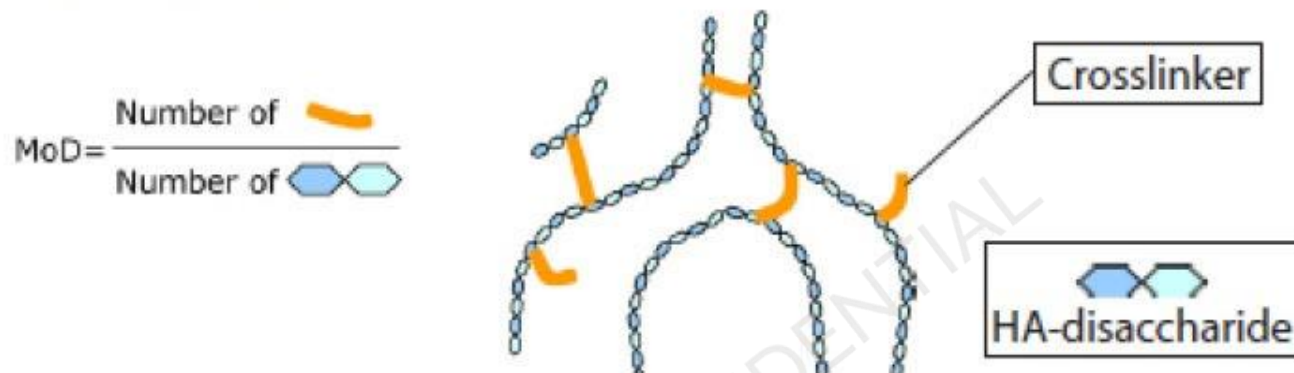


KYSENSE® is manufactured using a very low % of BDDE vs the HA filler industry

KYSENSE® has a very low Degree of Modification (MoD) compared to the market leading products

Degree of Modification (MoD)

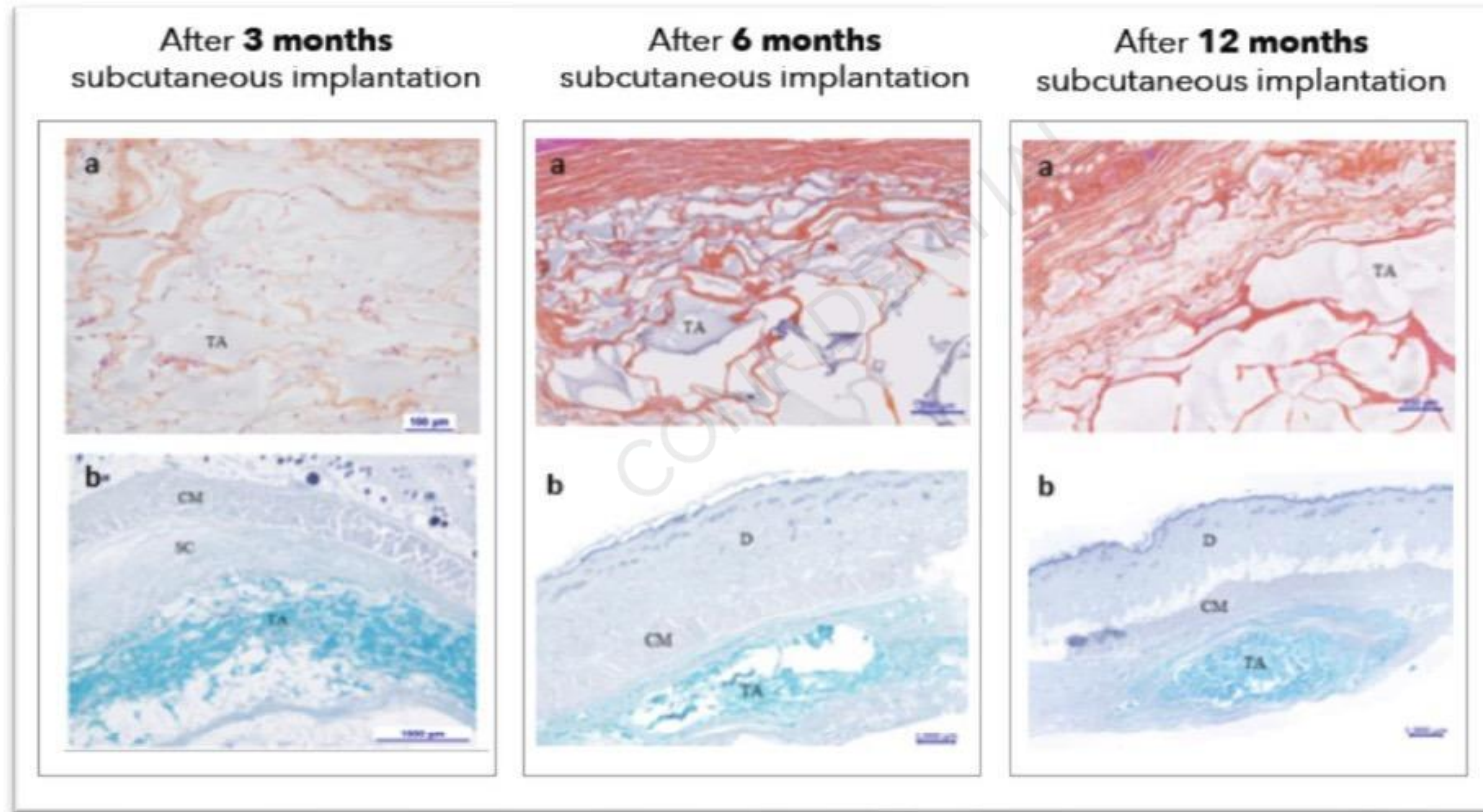
The degree of modification (MoD) is defined as the ratio of moles (number of molecules) of linked crosslinker to moles of HA-disaccharides. To preserve biocompatibility of the HA molecules the modification should preferably be kept at a minimum.



Product	Manufacture	MoD(%mol/mol)	Reference
KYSENSE® whole range	r KYLANE	<4	*
JUVEDERM® Ultra 3	ALLERGAN	7	**
JUVEDERM® Voluma	ALLERGAN	6	*
BELOTERO® Intense	MERZ	5.5	**
BELOTERO® Volume	MERZ	8	*
TEOSYAL® Deep lines	TEOXANE	8.5	**
TEOSYAL® Ultra Deep	TEOXANE	9	**

This means KYSENSE® maintains HMW (High Molecular Weight) in a supple matrix, is not as highly crosslinked and therefore is a highly flexible structure with *the ability to move as one with the surrounding tissue*

Over 12 months, KYSENSE® appeared as a homogenous 'gel like' material that is well integrated in the tissues. The material was colonized by variably thick bundles of mature collagen, demonstrating the proper tissue integration of the gel. **No markers of inflammation were observed at any time point**



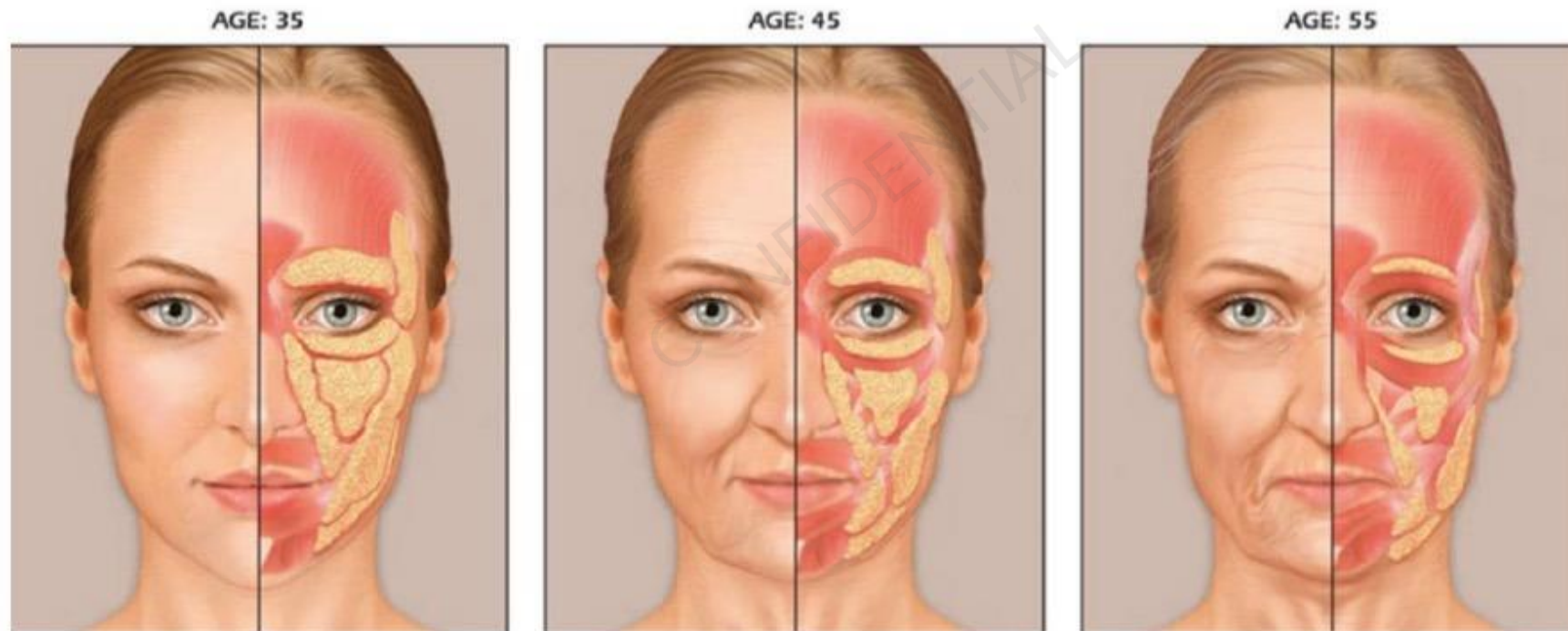
Biocompatibility test objective	Test Standard	Results
Test for in vitro cytotoxicity	ISO 10993-5	No evidence of cytotoxicity
Test for intracutaneous reactivity (irritation)	ISO 10993-10	No evidence of skin irritation (erythema, edema, necrosis)
Test for sensitization (hypersensitivity)	ISO 10993-10	No evidence of delayed dermal contact sensitization
Test for acute systemic toxicity	ISO 10993-11	No evidence of systemic toxicity for up to 3 days after implantation
Pyrogen test	European Pharmacopeia 2.6.8	No evidence of pyrogenicity
Test for subchronic toxicity	ISO 10993-11	No evidence of toxicity or signs of irritation or inflammation for up to 3 months after implantation
Test for genotoxicity: Ames test	ISO 10993-3	No evidence of genotoxicity
Test for genotoxicity: Mouse lymphoma assay	ISO 10993-3	No evidence of genotoxicity
Tests for local effects after intradermal implantation	ISO 10993-6	No evidence of irritation or minor local tissue reaction for up to 3 months, 6 months and 12 months after intradermal implantation
Tests for local effects after subcutaneous implantation	ISO 10993-6	No evidence of irritation or minor local tissue reaction for up to 3 months, 6 months and 12 months after subcutaneous implantation

Formulation	precise	define	volume	extreme
HA Concentration	15mg/ml	18mg/ml	21mg/ml	24mg/ml
Injection Depth	Dermis and Lip Mucosa	Deep Dermis and Lips	Subcutaneous fat tissue and supraperiostic zone	Deep subcutaneous tissue and supraperiostic zone
Volume per Syringe	1ml	1ml	1ml	1ml
Needles per Box	4 x 30g TSK HPC	4 x 30g TSK HPC	4 x 27g TSK HPC	4 x 27g TSK HPC
Syringes per Box	4	4	4	4

Considerations from the scientific panel
who developed KYSENSE®

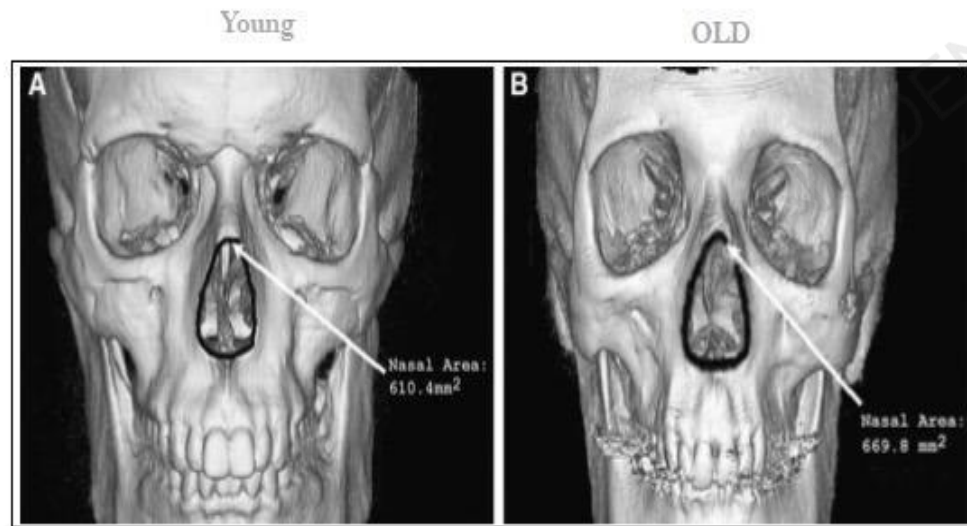
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Fat atrophy deflation



Bony resorption

... but bony resorption is also a major cause of the facial aging process.



Facial muscles provide high level of forces with different directions

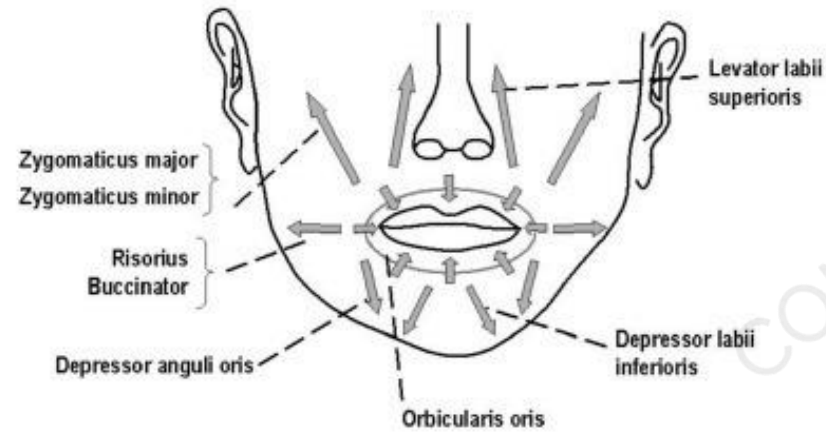


Fig. 2. Main directions of deformation that are important for the production of facial expressions (Hardcastle, 1976).

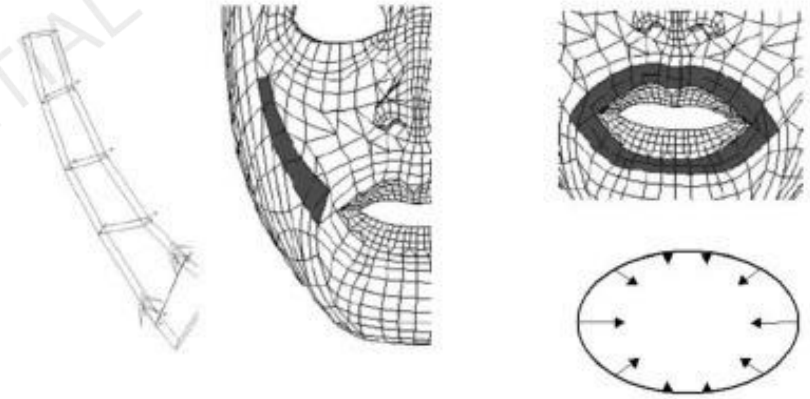
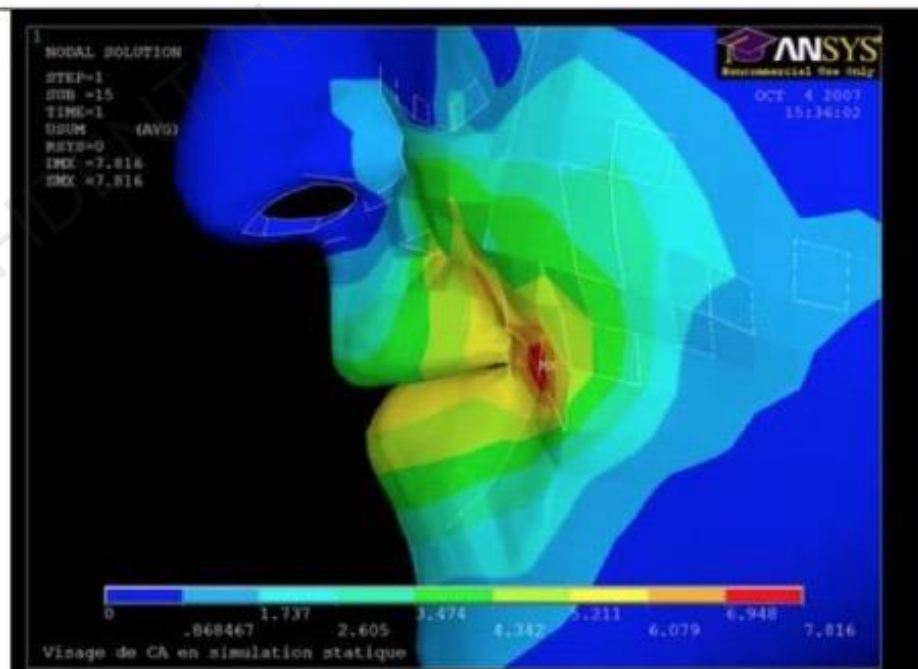
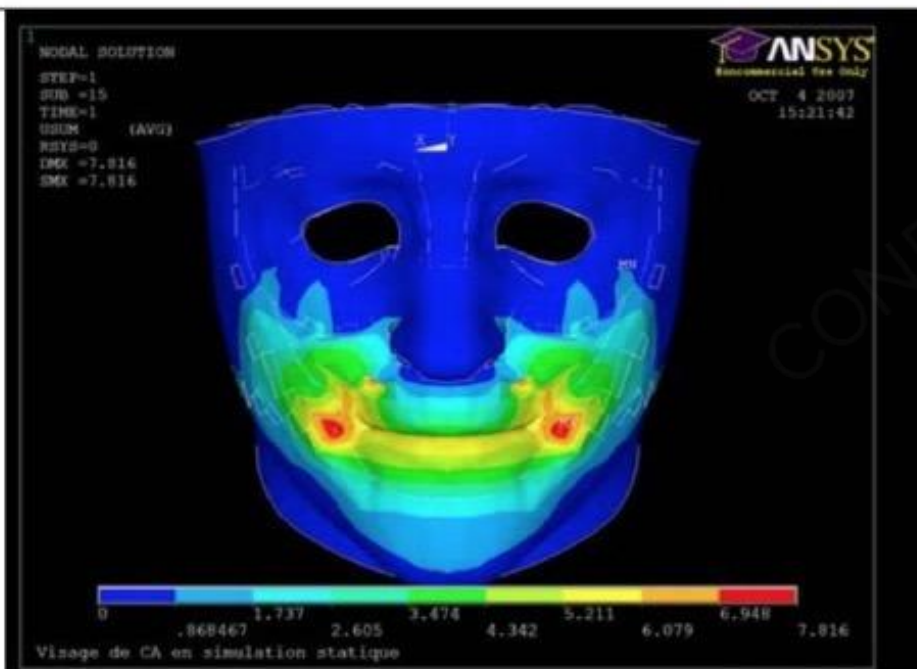
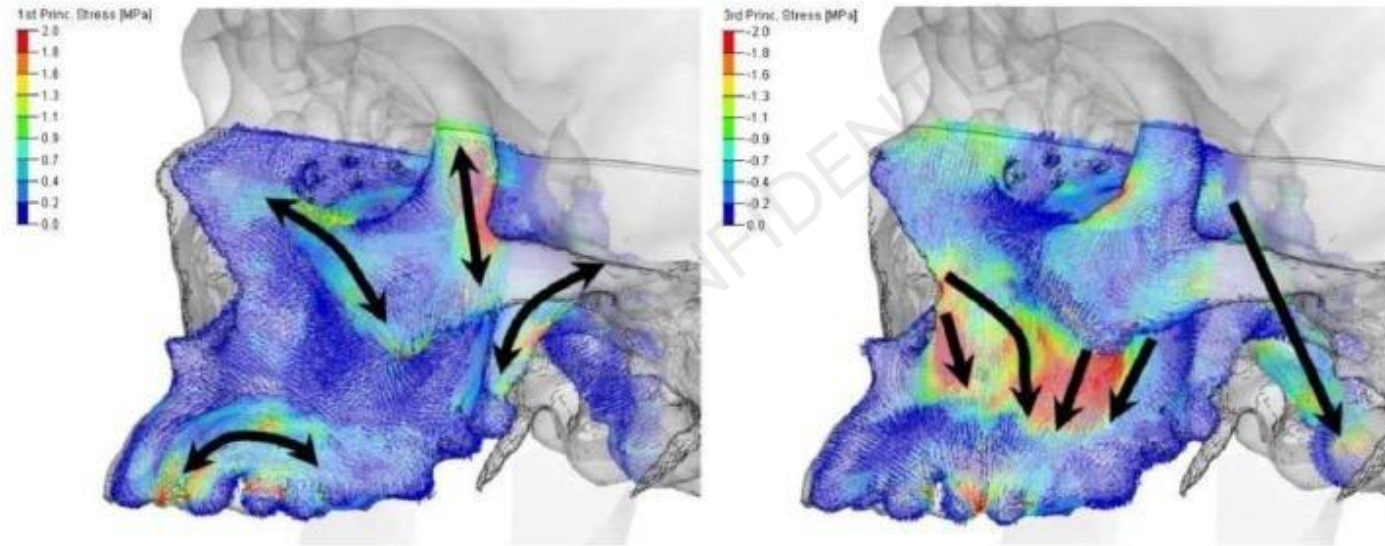


Fig. 5. Level of forces generated for two muscles. Left, a classical skeletal muscle, the Zygomaticus major. Right, the Orbicularis oris muscle, with a sphincter action.

Inducing deformation on facial tissue



Different constraints on facial tissue: Shear stress and Compression stress



Shear stress (left) and compression stress (right) under bite force

The scientific panel investigated these forces further to identify the 4 key rheological properties needed for the next advancement in filler technology:

“Key Rheological Properties of HA Fillers;
from
tissue integration to product degradation”

AUTHORS: Dr GavardMolliard, Bon Betemps, Hadjab,

Topchian,
Study identifies the 4 KEY RHEOLOGICAL PARAMETERS needed to
optimize aesthetic outcomes, safety and patient satisfaction
Micheels, Salomon

Plastic Aesthetic Research 2018; 5:17
*=Viscosity, Static Compression,
Shear Stress, Dynamic Compression*

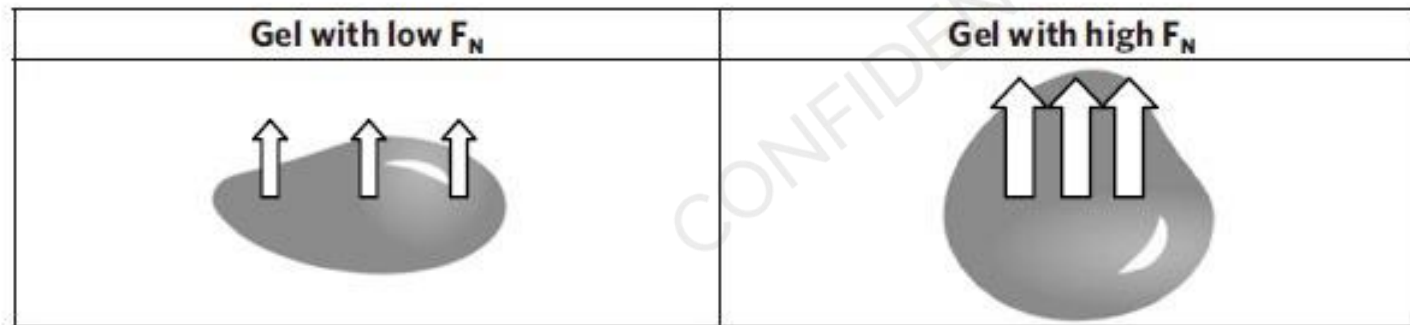
Key parameter 1 –Viscosity

η

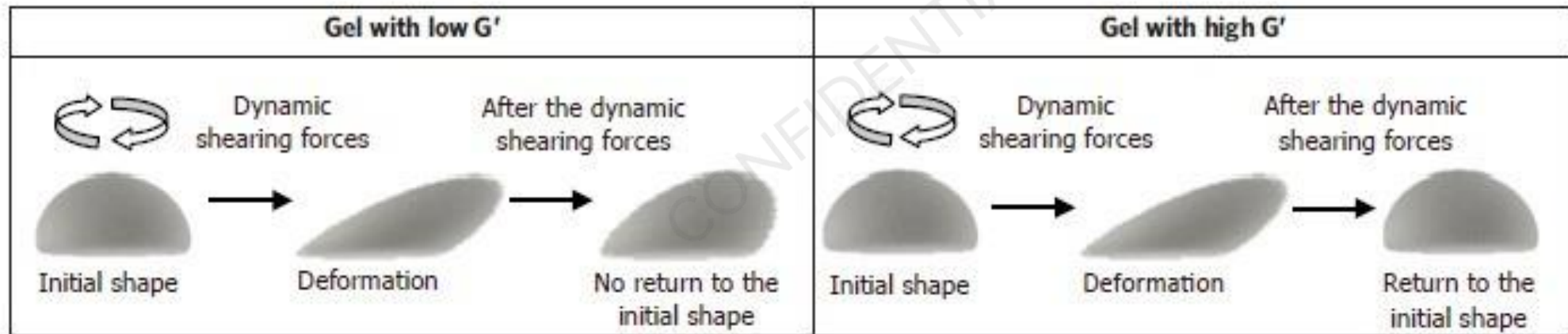
Gel viscosity	Cohesive gel	Non cohesive gel
Gel with low viscosity		
Gel with high viscosity		

Figure 1. Schematic representation of the cohesivity and viscosity of a HA gel. Impact of the cohesivity and viscosity on the shape and behavior of the gel

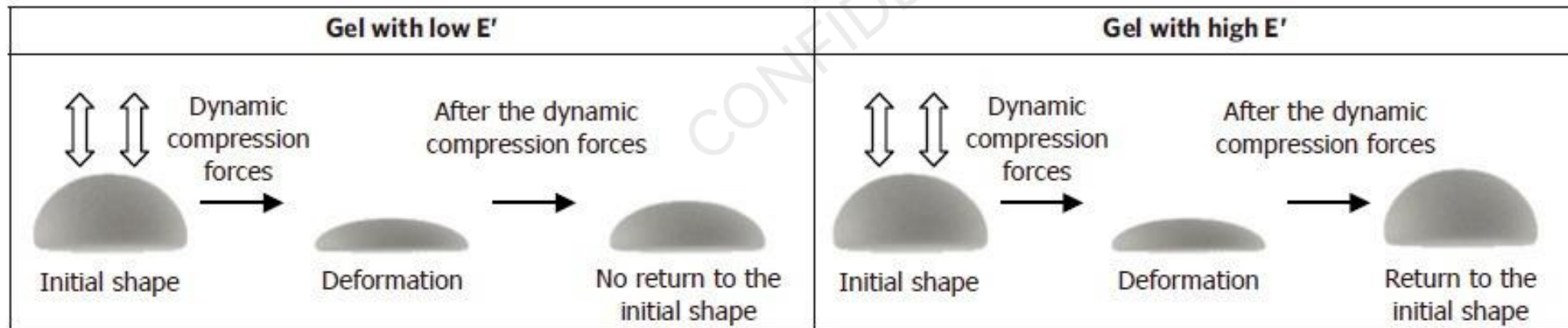
Key parameter 2 –Static Compression to measure projection force F_N



Key parameter 3 –Shear stress test to measure elastic modulus G'



Key parameter 4 –Dynamic Compression to measure elastic modulus E'



Results:

PRODUCT	VISCOSITY	STATIC COMPRESSION	SHEAR STRESS 'G'	DYNAMIC COMPRESSION
KYSENSE PRECISE	58 ±0	12 ±1	137 ±1	36080 ±1050
KYSENSE DEFINE	95 ±2	21 ±2	192 ±3	50130 ±1330
KYSENSE VOLUME	158 ±11	43 ±4	248 ±3	67021 ±1569
KYSENSE EXTREME	204 ±12	71 ±7	310 ±4	85765 ±1701
JUVEDERM VOLUMA*	65 ±1	15 ±2	318 ±3	59000 ±1440

Influence of rheological properties at each step of a fillers clinical lifetime

Table 3. Key rheological properties of HA fillers all along their clinical lifetime. Influence of viscosity η , normal force F_N , elastic modulus G' , elastic modulus E' and cohesivity at each step of the HA fillers' clinical lifetime

	Viscosity η	Normal force of compression F_N	Elastic modulus in shear-stress G'	Elastic modulus in compression E'	Cohesivity
Step 1: injection & integration	Major				Major
Step 2: projection		Major			
Step 3: dynamic facial expression			Major	Major	
Step 4: degradation	Major	Major			Major

Projection capacity assessment of hyaluronic acid fillers

AUTHORS: Jérémie Bon Betemps⁽¹⁾, Francesco Marchetti ⁽²⁾, Tingsong Lim⁽³⁾, Bassem Hadjab⁽¹⁾, Patrick Micheels⁽⁴⁾, Denis Salomon ⁽⁵⁾, Samuel Gavard Molliard ⁽¹⁾

Plastic and Aesthetic Research Bon Betemps *et al. Plast Aesthet Res* 2018;5:19

1. Research and Development Department, Kyane Laboratoires S.A., Plan-les-Ouates 1228, Switzerland.
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3. Clique Clinic Private Practice, Petaling Jaya 46300, Malaysia.
4. Dr. Patrick Micheels Private Practice, Genève 1206, Switzerland.
5. Clinique Internationale de Dermatologie Genève S.A. Private Practice, Genève 1201, Switzerland

This study applied 1) rheological testing and 2) a new skin model assay to evaluate projection capacity of both KYSENSE® Extreme and Juvederm® Voluma*

–1) Rheological Testing Result –Viscosity and Static Compression is significantly higher for KYSENSE® Extreme (Gel D)

Table 2. Key rheological properties of two HA volumizers

Product reference	Viscosity η at 1 s^{-1} (Pa.s)	Normal force F_N of compression at 0.9 mm^{-1} (cN)	Elastic modulus G' in shear stress at 1Hz (Pa)	Elastic modulus E' in compression at 1Hz (Pa)
Gel D	204 ± 12	71 ± 7	310 ± 4	$85,765 \pm 1701$
Juvederm Voluma	65 ± 1	15 ± 2	318 ± 3	$59,000 \pm 1440$

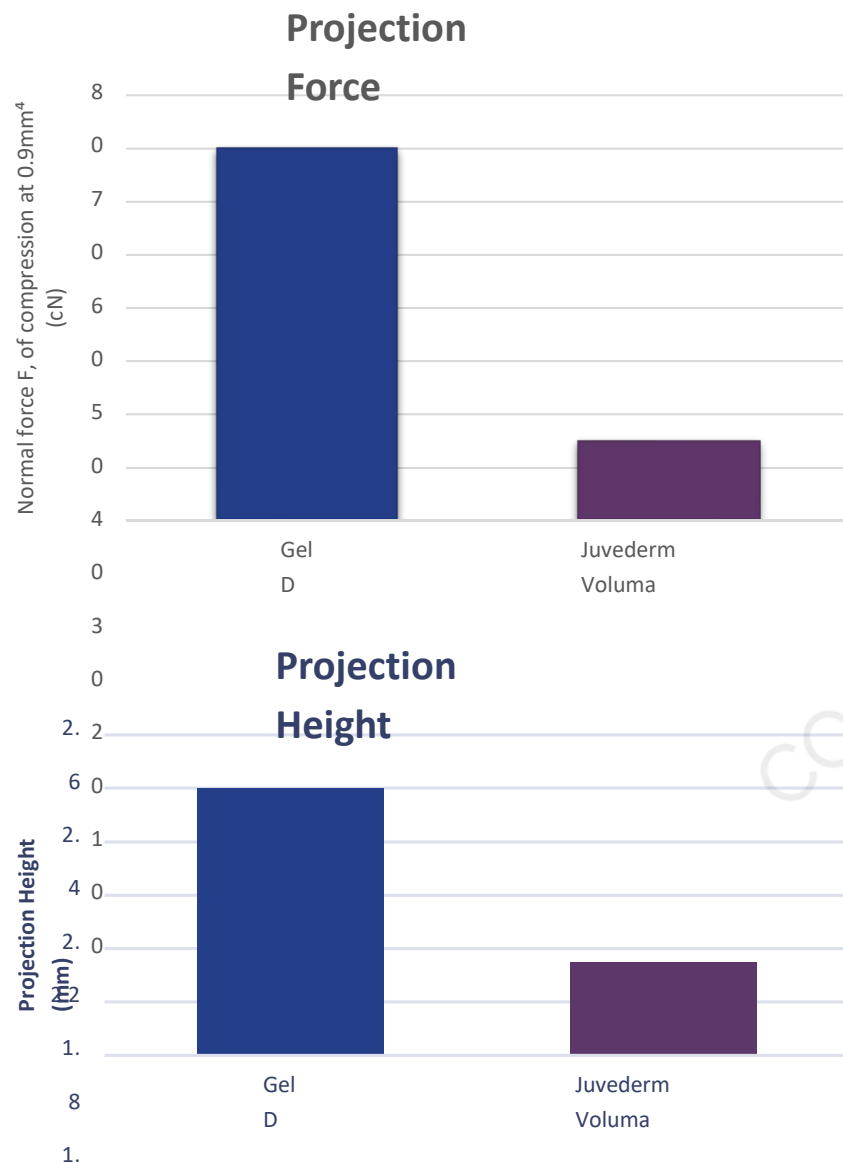


Figure 2. Rheological properties and projection heights of two HA volumizers. A: graph of projection forces for the 2 HA gels; B: picture of the projection heights with the 2 HA gels; C: graph of the projection heights for the 2 HA gels

2) Skin Model Assay

- Artificial skin model (Limbs and Things, Bristol, UK) composed of multiple tissue layers
- After peeling back the upper skin layer, 0.8g of each HA gel was deposited and the skin layer was layered back over the gel -
- Standardized photos at a distance of 30cm were taken
- The projection height induced by each HA bolus was measured in millimetre

Product reference	Projection heights (mm)
Gel D	2.38 ± 0.07
Juvéderm Voluma	1.77 ± 0.08

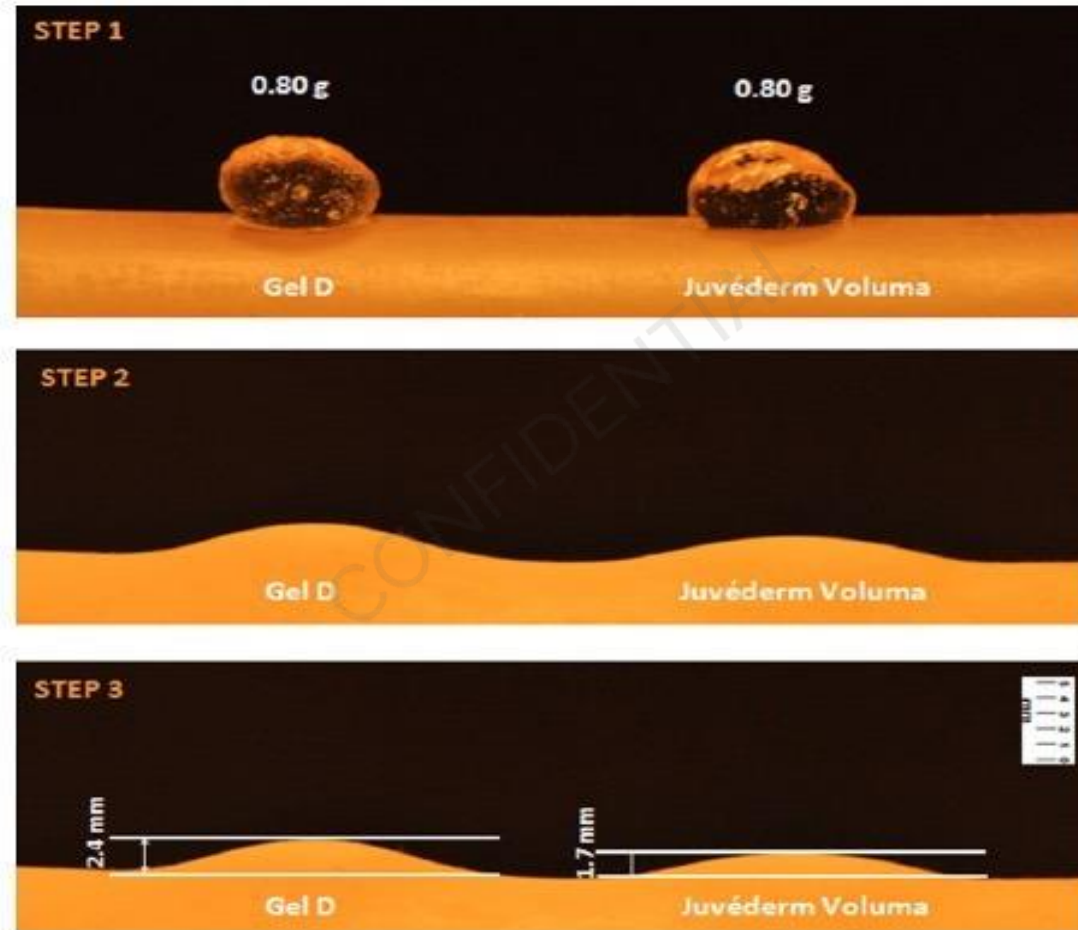


Figure 1. Illustration of projection heights measured with the skin model assay. Step 1: deposit of the tested HA gels; step 2: HA gels are overlaid by the upper skin layer; step 3: measurement of the projection heights induced by each HA gel

KYSENSE® Extreme exhibits 34% more
projection height compared to
Juvederm® Voluma

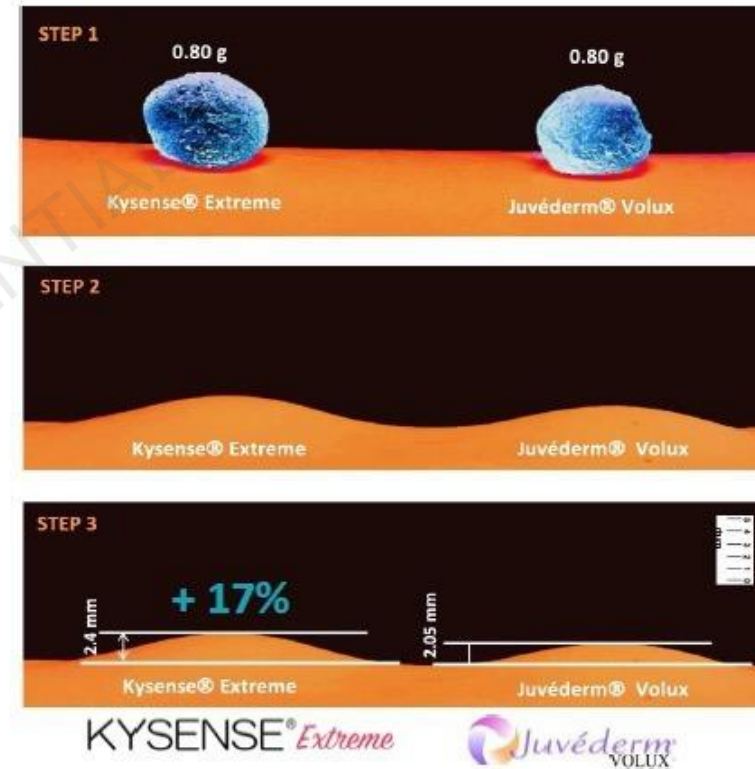
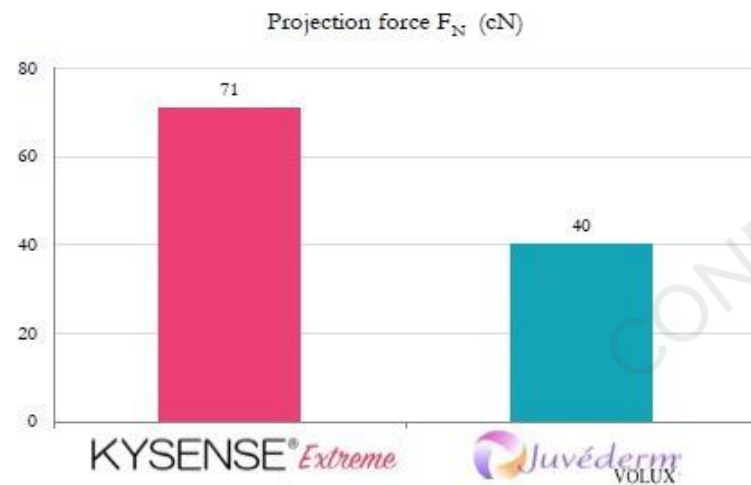
*statistically significant

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And when compared to Juvederm® Volux(HA
25mg /ml)

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Comparison of Extreme vs J. Volux

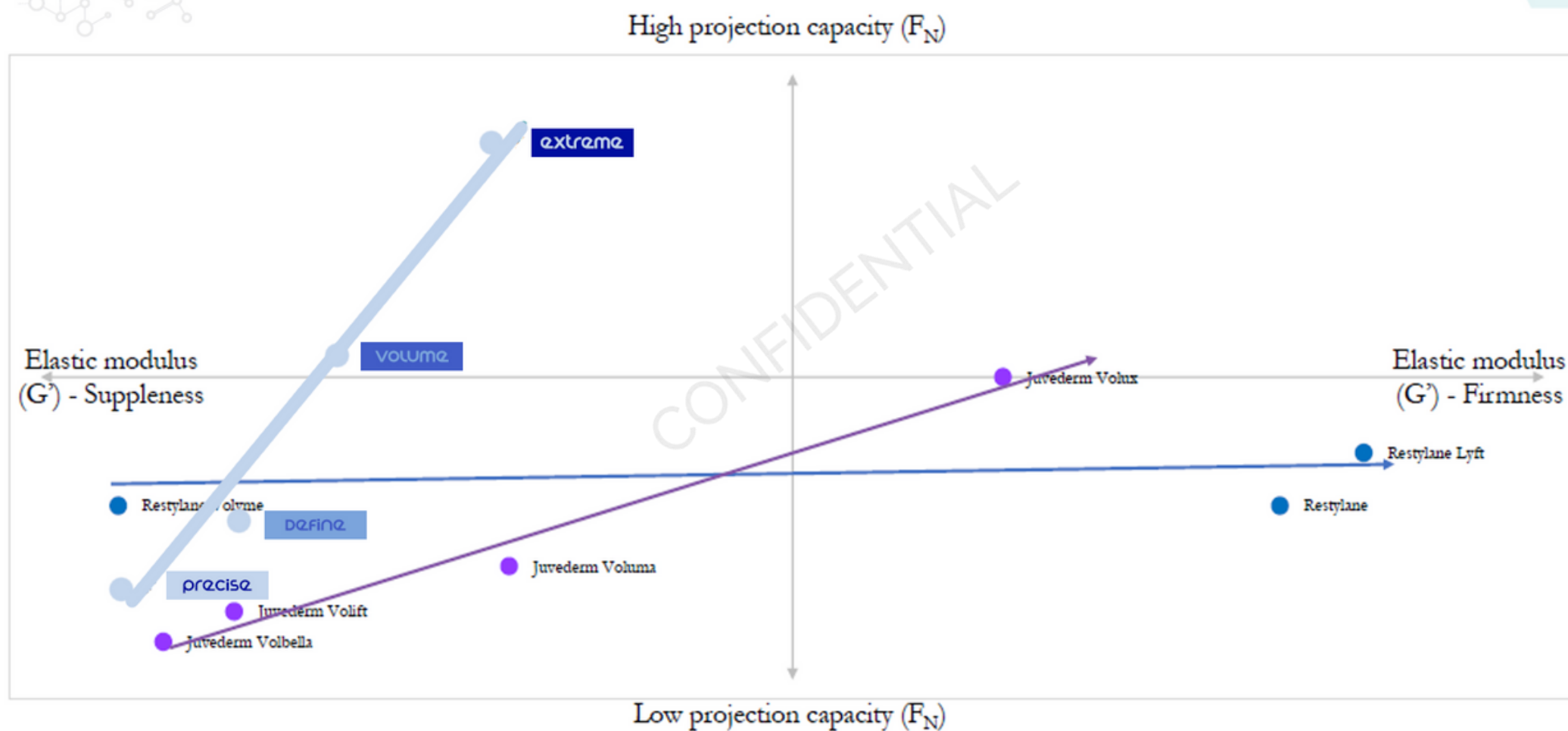


KYSENSE® Extreme exhibits 17% more
projection height compared to
Juvederm® Volux

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This results in....

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USABILITY OF KYSENSE®

Each product of the KYSENSE® collection is packaged in 1 ml COC plastic syringe (Schott syringe) with integrated luer-lock

TSK HPC needles provided in the KYSENSE® box have a 60% bigger inner diameter, this allows the best possible flow rate for a smoother extrusion force and more controlled injection. Needles are thin and ultra sharp, TSK show the lowest traumatic effect for the patient (TSKlab.com)

The hard polymer HPC advanced hub improves flow rates and allows for a tighter luer lock connection due to built in exterior threading. No flexing, no needle pop off (TSKlab.com)

Combined with comfortable finger grip and plunger rod from Dubourgel.



DUBOURGEL
médical

Extrusion force for each KYSENSE® SKU

Product	Manufacturer	Extrusion force (N) (@13mm/min)
Precise 30G	KYLANE	21.0
Define 30G	KYLANE	17.8
Volume 27G	KYLANE	14.5
Extreme 27G	KYLANE	17.6

Extrusion force for other fillers for comparison

Product	Manufacturer	Extrusion force (N) (@13mm/min)
BELOTERO® Balance 30G	MERZ	29.9
BELOTERO® Intense 27G	MERZ	25.7
TEOSYAL® Ultra Deep	TEOXANE	26.5
25G STYLAGE® XXL 30G	VIVACY	21.9
Juvederm® Voluma27G	ALLERGAN longer syringe	8.0

This comparison shows that the KYSENSE® products, injected with 30G or 27G needles, have comfortable extrusion forces for the Injector.

This fact was confirmed by:

- Swiss Dermatologists and Plastic Surgeons during the Product Development (injections into animal & human ex vivo tissues).
- Important to have products easy to inject for the usability and ergonomics, but also “not too easy” for achieving the best clinical outcomes in terms of safety & performance
- A “too easy” injection is not considered as the best option because the speed of injection can induce more dilacerations of the skin tissues (*thus generating more pain, more inflammation, more damage to extracellular matrix*) and more diffusion of the HA material in the treated area(= *partial loss of injection precision and volumizing capacity*).

-And the Injectors in the CE study ranked the ease of injection as “very satisfied” or “satisfied” for 100% of the performed injections with the KYSENSE® products.

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CE MARKED under the MDR by notifying body 2797 BSI Group Netherlands
Study 17E1176

Approved by the National French Health Authorities (ANSM) and the Ethics Committee and was performed on a cohort of 50 patients in France from March 2018 to March 2019.

Seven indications were treated with the whole KYSENSE® range*

No touch-up and no retreatment procedures were performed at any timepoint.

6 investigators were involved in the clinical study (5 injectors and 1 independent assessor).

The statistical analysis was finalized on the 14th of May 2019.

**HyalorogelB (KYSENSE® with the addition of lidocaine was used in this study)*

KYSENSE® clinical study

- * Randomised study split into 4 groups.
- * Age range 39-65yrs. 44 Female 6 Male subjects.
- * Open study for groups 1-3 and double blind for group 4 (Extreme)
- * 50 patients
- * Group 4 KYSENSE® Extreme VS Juvederm® Voluma involving 40 injection sites in split face for the treatment of the cheek area

INDEPENDENT ASSESSOR observed an aesthetic improvement (GAIS) in 95% of injected sites one month after treatment.

Six and twelve months after injection, respectively 93% and 81% of subjects still had an improvement according to the independent assessor.

SUBJECTS observed an aesthetic improvement (GAIS) in 97% of injected sites one month after treatment.

Six and twelve months after injection, respectively 94% and 90% of the subjects still had an improvement.

INJECTORS were 'very satisfied' to 'satisfied' regarding the ease of injection, the ease of product positioning, the immediate and after massage results for all devices.

No significant differences were observed between KYSENSE® Precise, KYSENSE® Define, KYSENSE® Volume and KYSENSE® Extreme in terms of performance.

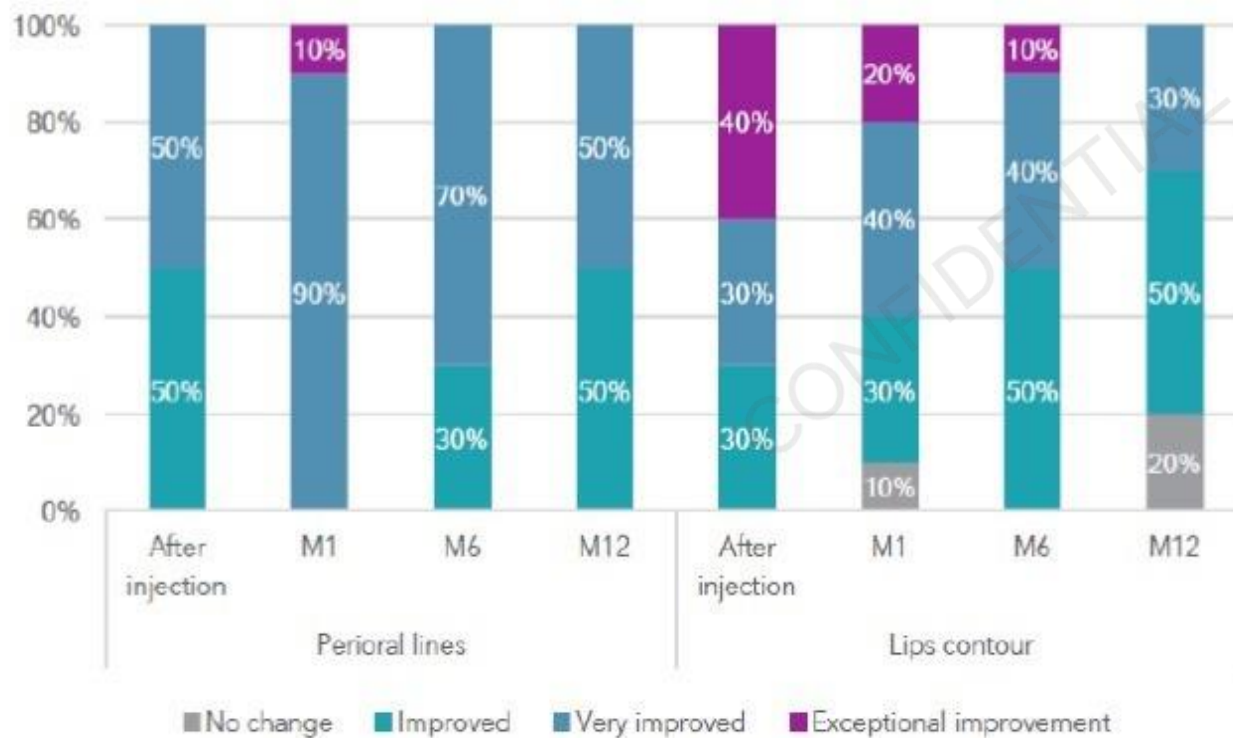
The 4 devices brought a global aesthetic improvement (GAIS) of at least 81% one year after injection.

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KYSENSE® Precise demonstrated high level of performance in peri-oral lines and lips contours. It is important to note that due to the high mechanical dynamics of the peri-oral area, these 2 indications represent a challenge for the treatment lasting.

Despite this fact, at 12 months, the assessor reported improvements for all subjects (100%).

Kysense[®] Precise : The long-lasting perioral HA filler



Before injection

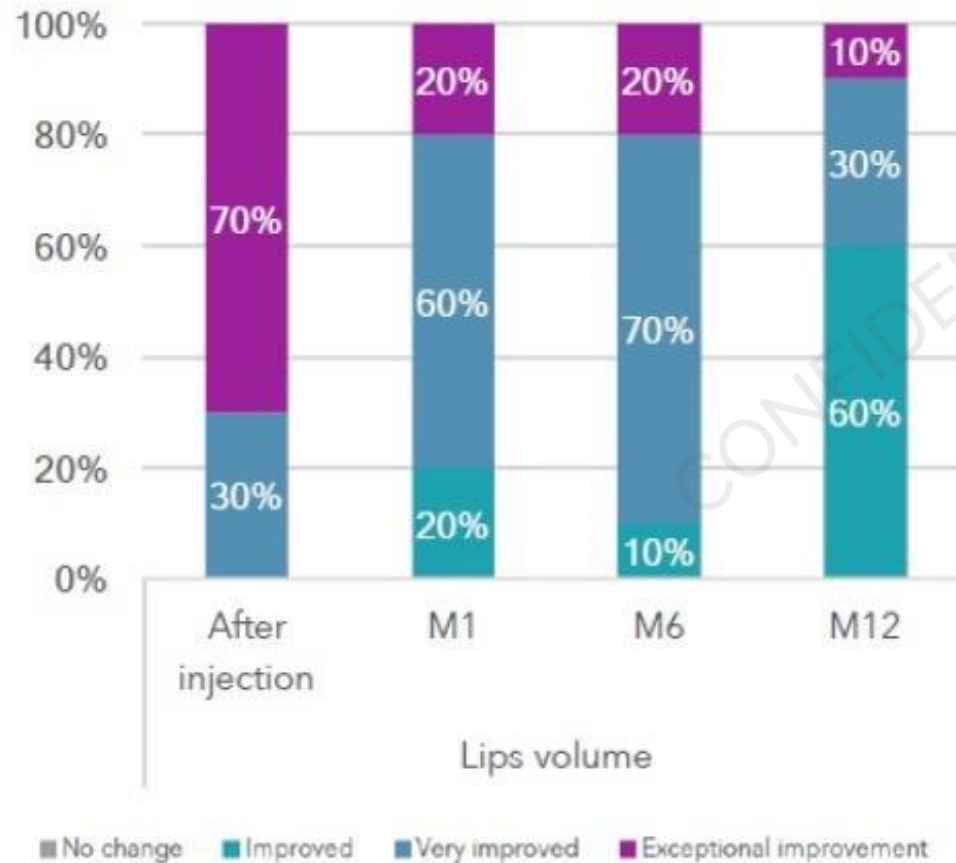


12 Months

KYSENSE® Define demonstrated high level of performance in lips volume augmentation and moderate nasolabial folds.

More specifically, the assessor reported global aesthetic improvements for all subjects (100%) at each timepoint of the clinical study.

Kysense® Define : The highly efficient lips volume HA filler



Before injection



1 Month



12 Months



KYSENSE® Volume demonstrated high level of performance in the treatment of severe nasolabial folds with an improvement rated by assessor of 85% after 12 months.

Kysense® Volume				
	D0 before injection	M1	M6	M12
Subject #301				
Subject #304				

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Comparison between the performance of KYSENSE® Extreme and JUVEDERM® Voluma:

Independent assessors were blind to the product and injectors were given no recommendation on injection volumes, just to treat to result.

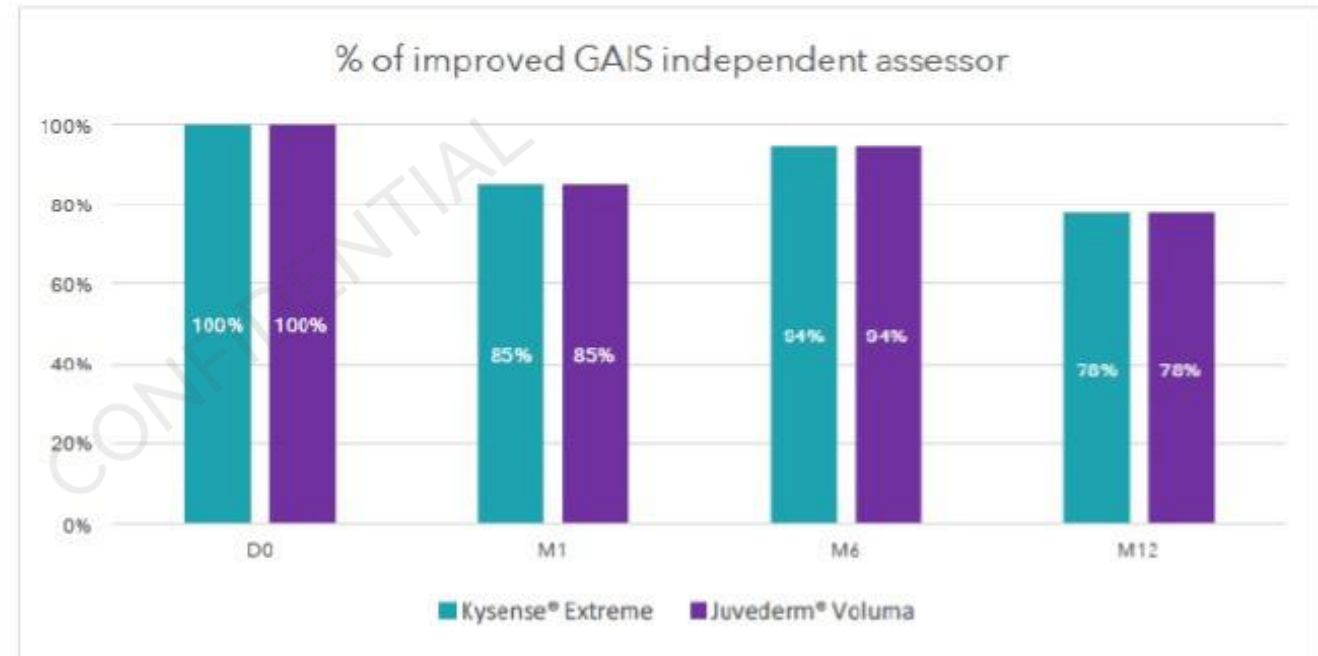
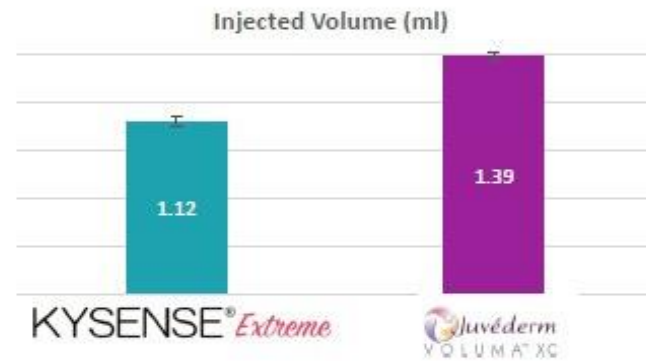
- Overall they injected less quantity of KYSENSE® Extreme (-24%) to achieve same result: significantly less than JUVEDERM® Voluma™

- The GAIS score rated by the blind assessor and the subject did not show any significant difference between the two devices in terms of results

- o The MFVDS score rated by the blind assessor did not show any significant differences between the two devices at all time points.

- o A mild significant difference in favor of KYSENSE® Extreme was observed regarding ease of product positioning, immediate results and results after massage rated by the injectors

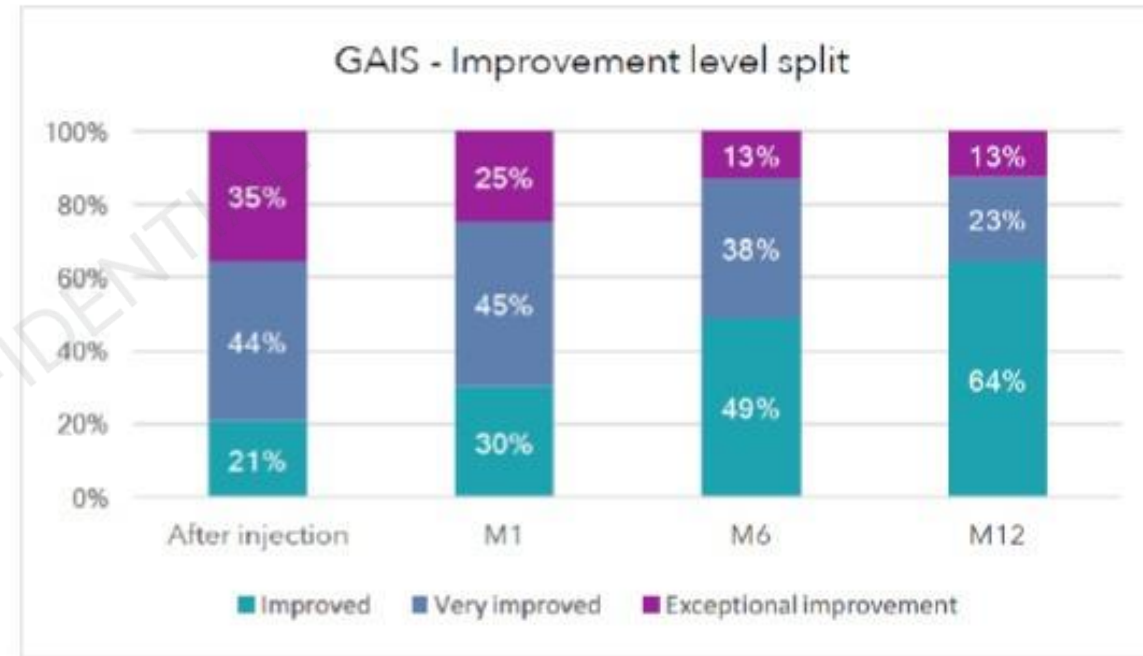
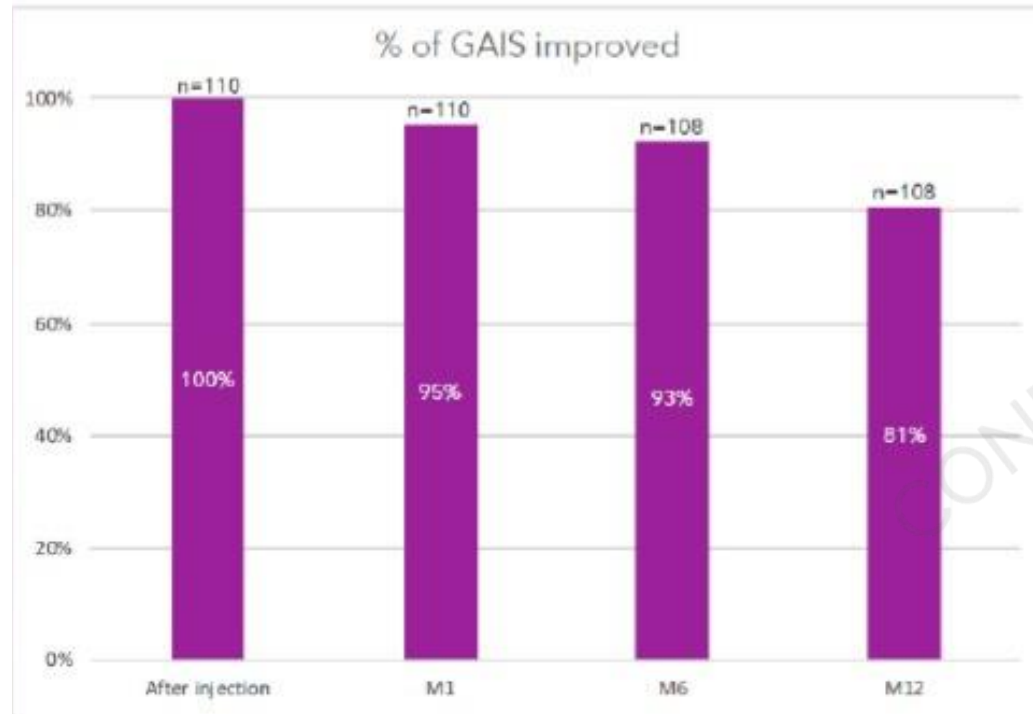
Kysense® Extreme, the super-volumizer HA filler



24% less product required with *Kysense® Extreme* to reach similar GAIS over time.

KYSENSE®

Very high performance on the overall range at 12 months

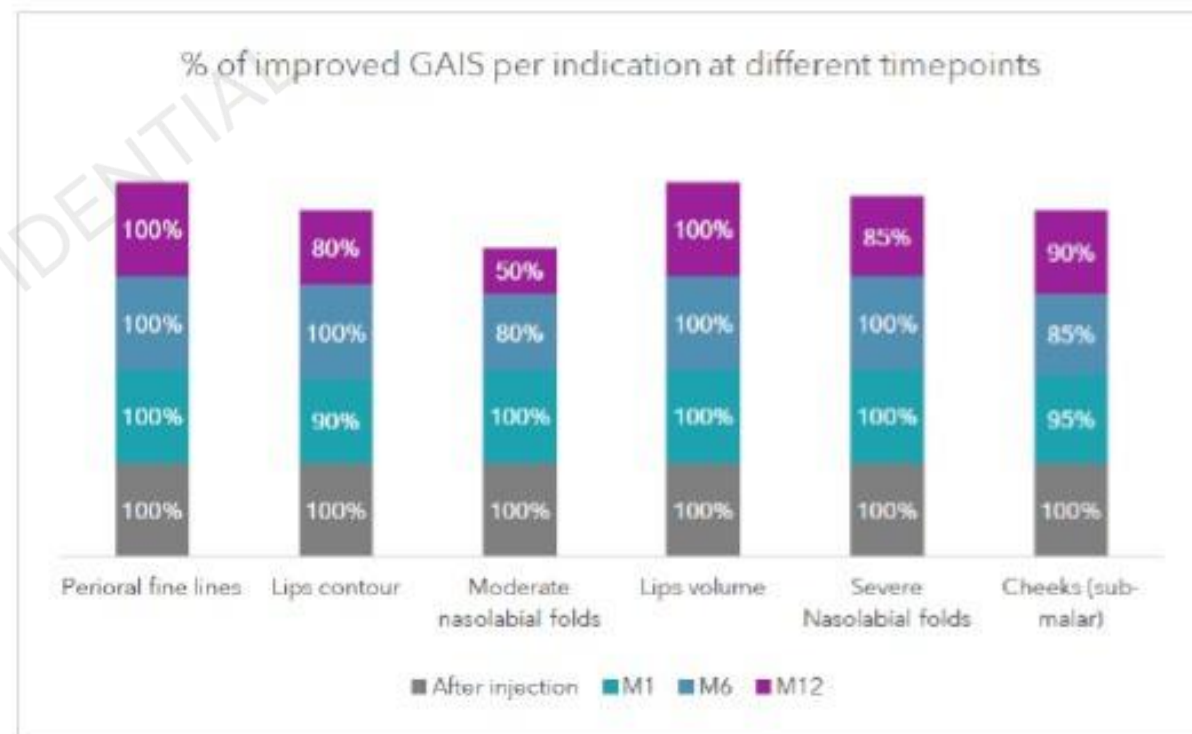
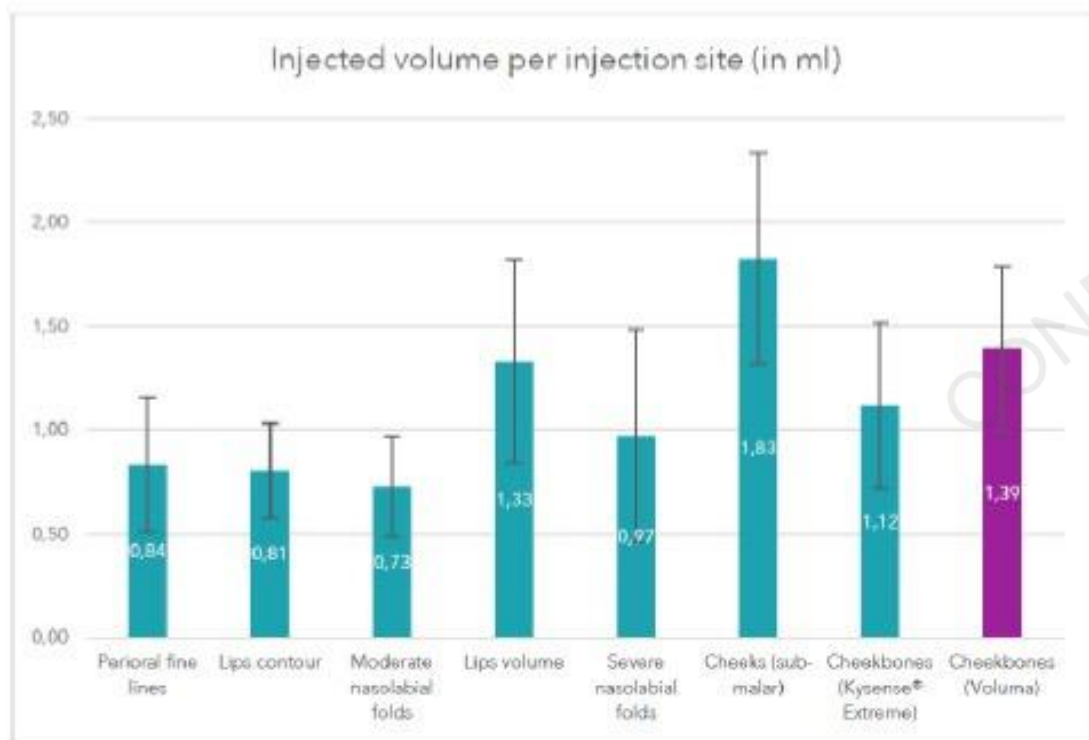


The whole Kysense® range exhibits **an impressive lasting up to 12 months.**

=> 81% of treated indications are improved, very improved or exceptionally improved.



Less is more™ concept confirmed on the whole range



Overall safety of the KYSENSE® range was evaluated using Injection Site Reactions (ISR) rated by the independent assessor at D0 after injection and at one month (M1).

All reported Injection Site Reactions ISR were usual signs observed with HA filler injections.

One month after treatment, most of the Injection Site Reactions occurring after the injection were resolved.

No Serious Adverse Event occurred during the study.

Post study monitored by French CRO (Clinical Research Organisation)

Summary:

- *A soft, supple filler that maintains high projection capabilities over time, less risk of migration
- *A natural looking and feeling filler that is well integrated into the tissue with zero inflammation
- *Only High Molecular Weight pharmaceutical grade HA is used to minimise inflammation
- *Carefully engineered extrusion forces for comfortable injection experience (user and patient)
- *Ultra sharp needles (TSK) lead to less pain on injection and less trauma to the tissue
- *Smooth product that does not dilacerate the tissue making the treatment more comfortable and leading to less swelling
- *Average 20-30% less product is needed, always treat to result (not to mL)
- *Very little free HA –do not over correct or over fill

KYSENSE® Tips and Tricks for use

Read the IFU in full -Instructions for Use -provided within each box of KYSENSE®

Use only the supplied ultra sharp TSK HPC needles (30G ½ Precise and Define and 27G ½ Volume and Extreme).

Extra accessories: Cannula 25G x 50mm / 22G x 50mm / 22G x 70mm. Luer-luer connector if you wish to mix lidocaine (0.1cc 2% lidocaine).

Ensure the hub of the needle is as tightly fixed to the bottom of the luer lock as possible and remove shield of the needle just before injection.

To avoid the plunger coming off when aspirating –please ensure the plunger is screwed in to the syringe driver and continue to monitor this during the injection especially if the syringe is turning and potentially loosening the plunger thread.

Injection technique should be smooth and slow, particularly for Volume and Extreme.

For optimal clinical results, gentle massage by the injector of the treated area is recommended to ensure uniform distribution of the material.

Formulation	precise	define	volume	extreme
HA Concentration	15mg/ml	18mg/ml	21mg/ml	24mg/ml
Injection Depth	Dermis and Lip Mucosa	Deep Dermis and Lips	Subcutaneous fat tissue and supraperiostic zone	Deep subcutaneous tissue and supraperiostic zone
Volume per Syringe	1ml	1ml	1ml	1ml
Needles per Box	4 x 30g TSK HPC	4 x 30g TSK HPC	4 x 27g TSK HPC	4 x 27g TSK HPC
Syringes per Box	4	4	4	4

Key objectives in the development of KYSENSE[®] -achieved

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KYSENSE®

Redefining the science and aesthetic of facial anatomy



extreme

volume

define

precise

KYSENSE®



Clinical indications
of the Kysense®
Hyaluronic Acid
Dermal Filler Range

KYSENSE®

precise

for skin texture and finishing

define

for facial dynamic expression

volume

for facial volumising

extreme

for facial sculpting and contouring

KYSENSE®

Thank you &
questions....