Journal of Clinical and Cosmetic Dermatology
ISSN 2576-2826 | Open Access

RESEARCH ARTICLE

Volume 6 - Issue 2

Effect of Adding Lidocaine to Hyaluronic Acid Gel for Volume Loss Correction: A Preliminary Observation

Patrick Micheels[1,*], Stéphanie Besse[2], Badwi Elias[3], and Joan Vandeputte[4]

[1]Private office, chemin de la Fontaine, Chêne-Bougeries, Switzerland
[2]Med Image, RX Institut: 1, route de Florissant, Geneva, Switzerland
[3]Private office, route de Florissant, Geneva, Switzerland
[4]Private office, Meerspoort, Oudenaerde, Belgium

***Corresponding author:** Patrick Micheels, Private office: 8, chemin de la Fontaine, 1224 Chêne- Bougeries, Switzerland, Tel: + 41 22 347 11 13; E-mail: patrickscab@bluewin.ch

Received: 26 Apr, 2022 | **Accepted:** 20 May, 2022 | **Published:** 27 May, 2022

Citation: Micheels P, Besse S, Elias B, Vandeputte J (2022) Effect of Adding Lidocaine to Hyaluronic Acid Gel for Volume Loss Correction: A Preliminary Observation. J Clin Cosmet Dermatol 6(2): dx.doi.org/10.16966/2576-2826.173

Abstract

Introduction: Although adding a local anesthetic is an effective way to reduce pain during intradermal Hyaluronic Acid (HA) injections, it is not clear if the pain control is as effective when performing injections close to the bone. The primary aim of these preliminary observations was to explore this issue. As a secondary aim, we wanted to assess if the addition of lidocaine alters the behavior of HA gel in the tissues over time.

Subjects: Two women provided informed written consent to participate in the study. Participants were blind to the type of HA gel used for either temporal fossa.

Methods: A cross-linked HA gel was used for the study. One side was injected with the gel with and the other without lidocaine, in no particular order. Photographs from the front, profile and three-quarter left and right and frontal MRI scans were taken before and just after the injections, then every 6 months for 2 years.

Results: The side injected with the gel with lidocaine was significantly less painful than that injected without lidocaine. Both types of gel changed shape on MRI in the first 6 months but stayed stable thereafter till the end of our follow-up at 24 months. Based on MRI, patient reported outcomes and expert assessed aesthetic outcomes, using MAS® and the global aesthetic improvement scale, both types of gel were comparable.

Conclusion: The addition of lidocaine to HA volumiser gels reduces pain to a remarkable degree.

Keywords: Volumiser gel; Lidocaine; Volume loss; IPN-Like; MRI; Temporal; Pain; MRI; MAS; GAIS

Introduction

Ageing process involves loss of fatty tissue, muscle and bone mass. With the exception of very thin people, a youthful face tends to have a generally convex appearance in women. As they age, the area around the temporal fossa begins to skeletonize. Apart from autologous fat, it is now feasible to use cross-linked hyaluronic acid gels as a filling agent to combat this loss in volume. Since its introduction, nearly 25 years ago, Hyaluronic Acid (HA) gels have become the most commonly used product for smoothing wrinkles [1,2]. Indeed, in the aesthetic industry, HA has become almost indispensable for correcting the loss of facial volume resulting from ageing.

The HA gels that we use come with or without lidocaine, an innovation initially introduced to the European market by *Juvéderm® Ultra 3* gel, containing lidocaine, in December 2007, which was later approved by the FDA (Food And Drugs Administration) [3]. It has been clearly demonstrated that adding lidocaine to HA gels significantly reduce patients' pain perception when their wrinkles are being filled, but without providing any real explanation of the ultra-fast efficacy of this addition in the dermis [3,4]. This rapid effect was observed at the time when bovine collagen was being used. It is currently not known if the same pain reduction benefit would also be experienced in the context of age-related volume loss correction, when the gel is injected as a bolus, deep into the muscle close to the bone in the temporal fossa. This issue is particularly relevant because it is possible that the periosteum covering the temporal bone disappears almost completely during a person's lifetime [5-8].

It is known from studies exploring HA tissue distribution when treating HIV- associated lipodystrophy that HA gel replacement of the lost fat has a lasting effect [9]. However, adding lidocaine can modify the rheological properties of a HA gel, and this in itself can,

potentially, modify its persistence over time [10]. The main aim of our preliminary observations was to check whether adding lidocaine to HA volumiser gels reduces the amount of pain experienced when injected deep, intramuscularly, close to the bone. Furthermore, we wanted to assess if the addition of lidocaine had an impact on the behavior and persistence of the gel over time, compared to the same gel without lidocaine.

Methods

Participants

Two white Caucasian women agreed to participate in this observational study in our private aesthetic center. Both subjects were provided with written and oral explanation of the procedure and study and given a 15-day cooling-off period prior to consenting to participate. The study was conducted in full compliance with the Helsinki declaration. Participants also had full rights for their images and were fully aware that they would not be used for any purpose without their prior full consent. The volumiser product was used within the recommended manufacturer and licensing indications and contraindications.

Procedure

A 26 mg/ml cross-linked HA gel developed using *IPN-Like* technology (Vivacy, Archamps, France) was used for the study. Based on the manufacturer's experiments, the gel is estimated to have cohesive properties ranging between 4.5 and 4.9 on the Sundaram J, et al. scale [11-13]. We used the following gels: *Stylage® XL* (without lidocaine). Batch: EXI18075F Exp.: 2020-08 and EXH18031F Exp 2020- 07 and *Stylage® XL-Lido* (with lidocaine). Batch: LXD16362F Exp.: 2019-05.

Not in any particular order, one side of the face was injected with the gel without lidocaine and the contralateral side with the gel with lidocaine. Participants were blind to the type of gel being injected. TSK $27G^{1/2}$ (0.4 × 13 mm) needles, included in the packaging provided with the gels, were used for the injections. The needle was inserted perpendicular to the skin surface, 1 cm from the temporal crest and 1 cm above the orbital rim until it touched the bone. The gel was then slowly injected as a bolus into the deep intramuscular area next to the bone in the antero-superior third of the temporal fossa [5-8]. If required, additional injections were given up to a maximum of 1.0 ml per side. The injected HA gel was then gently massaged by hand to spread them out uniformly.

MRI

These were performed using an Achievia scanner 1.5 Tesla (Philips SA Health Systems, Gland-Switzerland). Imaging was performed in the medical imaging institute MedImage, Geneva, Switzerland. The lasting effects of both gels were independently and objectively measured using time-lapse MRI over a 24-month period. Prior to any injection a frontal MRI scan was taken in order to evaluate the situation at baseline. A 2nd MRI scan was performed immediately after the injection and massage. MRI scans were then carried out at 6, 12, 18 and 24 months. These latter scans were used to assess the behavior of the gels, any spreading into the adjacent tissue over time and monitor gel resorption over the follow-up period. Evaluations were independently carried by a radiologist who was blind to the type of gel used in the side of the face being assessed. The MRI sequences used were 3DFLAIR, 3DT1, 3DT2. The residual volume was calculated using a tool integrated into the Philips IntelliSpace Portal 7.0 image post-processing software, which can display and measure volumetric data from the captured 2D images.

Photographs

Frontal, profile and three-quarter right and left photographs were taken before each treatment, immediately after, and then at 6 monthly intervals for 2 years. A digital camera was used for the baseline and follow-up photographs (*Nikon®* DX, lens AF-S DX Nikkor, ED 18-55mm 1: 3.5-5.6 GII).

Patient reported and clinical outcomes

Participants were asked to evaluate the intensity of their pain perception during injection (T0) then immediately after (T1), 5 minutes after injection (T2), 30 minutes after injection (T3) and at home (T4) using a 0 -10 Visual Analog Scale (VAS) where 0=no pain and 10=unbearable pain.

Aided by the digital photographs, participants' perception of the quality of the aesthetic result were assessed by means of the MAS© visual scale, Merz-Pharma [14] (Figure 1) and the Global Aesthetic Improvement Scale (GAIS), which were self- completed immediately after treatment and at 6, 12, 18 and 24 months post procedure. GAIS is a 5 point scale ranging from 0 - 4 and corresponds to deterioration, no change, visible improvement but requires a 2nd treatment, clear improvement but not optimal and optimum treatment. Additionally, the treating physician and three independent experts used these photographic images to assess aesthetic outcomes at the same time points. The independent experts were blind to the type of gel used in the side of the face being assessed. Similar to participants, the GAIS and MAS© scales were used for the assessments.

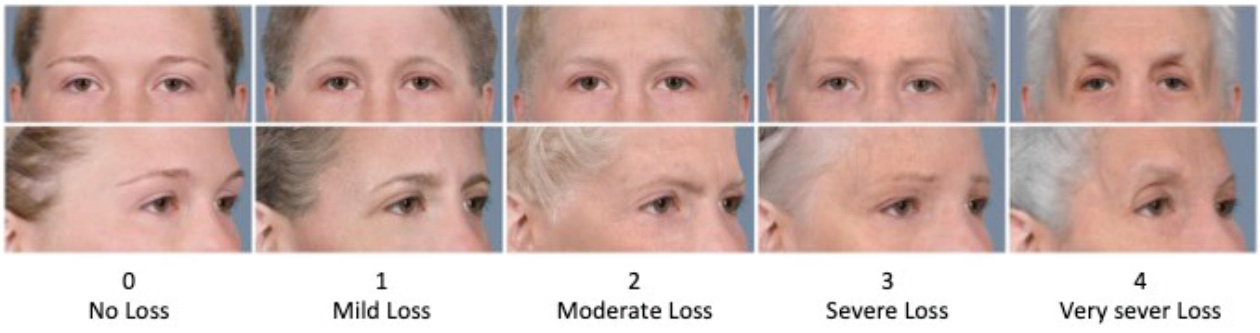

Figure 1: Visual analogue assessment for ageing of the temple according to the MAS© Merz- Pharma scale (COURTESY MERZ® Pharma).

Results

The 2 participants were 71 and 58 year old and their skin types were III, III and II, III according to Fitzpatrick's classification [15] and Glogau scale [16] respectively. The injection side and the participants' rated VAS pain score for each injection site at the different pre-set time points are presented in table 1 for both participants.

Based on the serial MRI images there was a difference between the two types of gels (*XL* and *XL-Lido)* with regards to their levels of resorption overtime (Figure 2). The MRI characterization of gel behavior and volume at different time-points is presented in table 1 and 2.

With regards to aesthetic outcomes, participant 1 reported a 2 point improvement on the MAS® scale compared to baseline for both the right and left sides immediately following treatment. This improvement persisted until the 12 months assessment. At 18 months, she considered that there was some deterioration, which was more on the *Stylage® XL-Lido* side, with 2-points worsening on the MAS® scale compared to 1 point on the right-hand side. Nevertheless, on her self-evaluation using GAIS she rated the left side as 3 (Clear improvement, but not optimal, perhaps a "touch-up" at 3 months) and the right side as 2 (Visible improvement, but requiring a 2nd treatment). However, at 24 months she perceived that there was a significant improvement again, with a 2-point improvement on MAS®, compared to her score at 18 months, for both sides and a score of 3 on GAIS for both sides (Table 3 and Figure 3).

Participant 2 reported a 1-point improvement on the MAS® scale for each side immediately after treatment. At the 6, 12 and 18 months follow-up she considered the improvement to be better where she scored a 2-point improvement compared to baseline. By 24 months the participant still considered there was an improvement in her volume loss but rated this as a 1-point improvement on the MAS® scale in comparison to before treatment. Nevertheless, she rated her aesthetic improvement as perfect on GAIS throughout (Table 3 and Figure 4).

Using the same scales and time points, individual and average experts' assessments of photographic images for both participants are presented in tables 4 and 5.

Discussion

We observed that adding lidocaine to a cross-linked HA gel developed using *IPN-Like* technology and intended for correcting facial skeletonization reduced the pain experienced by patients at the time of injection despite its depth. Indeed, both participants felt almost no sensation during the Stylage® *XL-Lido* compared to XL injections (1/10 on the VAS scale, compared to 6/10 at T0). Furthermore, both participants reported no pain by 5 minutes in the *XL-Lido* injection sides.

During the follow-up we demonstrated that the aesthetic results of *Stylage® XL* and *Stylage® XL-Lido* gels for the correcting age-related volume loss were comparable. For participant 1 and based on the

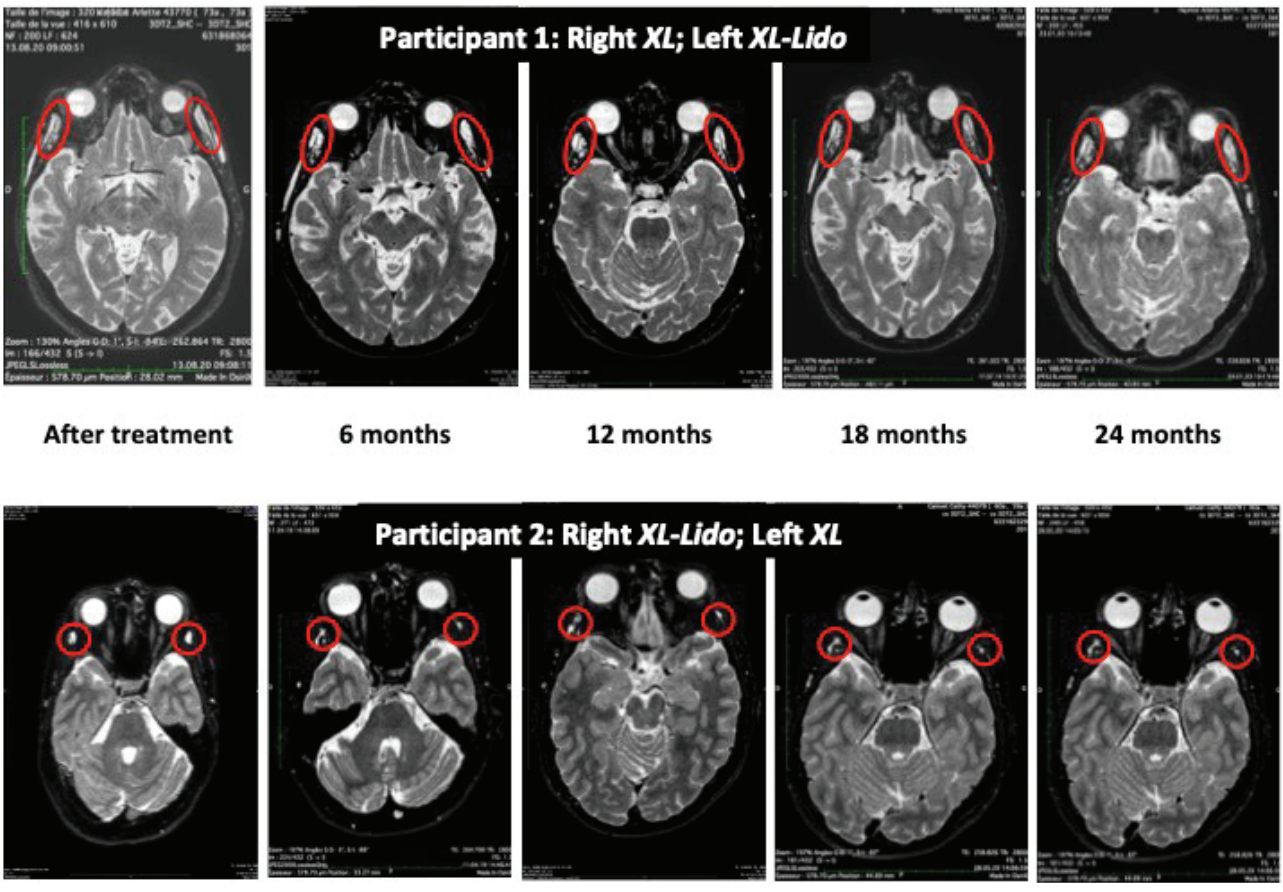

Figure 2: Serial MRI images for both participants.

Figure 3: Participant 1: Photographs before treatment (BT) and at 12 months follow-up (M12).

Figure 4: Participant 2: Photographs before treatment (**BT**) and at follow-up.

Table 1: Pain scores for different gel types at different time points.

			Right Temple	Left Temple
Participant 1	**Gel Type (Volume)**		***Stylage®XL,* (1.0 ml)**	***Stylage®XL-Lido* (1.0 ml)**
	Pain Scores	T0	6/10	1/10
		T1	5/10	0/10
		T2	2/10	0/10
		T3	1/10	0/10
		T4	0/10	0/10
Participant 2	**Gel Type (Volume)**		***Stylage®XL-Lido* (0.55 ml)**	***Stylage®XL* (0.50 ml)**
	Pain Scores	T0	1/10	6/10
		T1	0/10	5/10
		T2	0/10	<3/10
		T3	0/10	2/10
		T4	0/10	0/10

T0: During injection; **T1:** Immediately after injection; **T2:** 5 minutes after injection; **T3:** 30 minutes after injection; **T4:** At home.

Table 2: MRI characterization of gel behavior and estimated volume at different time points.

		Right Temple	Left Temple
Participant 1		***Stylage®XL, without lidocaine* (1.0 ml)**	***Stylage®XL-Lido* (1.0 ml)**
	AT	Gel in the form of a papule with a linear appearance, a dense uniform structure and convex edges located mainly under the aponeurosis, not touching the bone, (770 mm^3).	Gel infiltrated underneath the aponeurosis, not touching the bone, no papule but with a dense uniform structure and concave edges (1,129 mm^3)
	M6	Gel extended antero-posteriorly, flattening out and infiltrating caudally (1,950 mm^3).	Gel became narrower and extended caudally (1,226 mm^3).
	M12	The gel had a stable appearance (1,571 mm^3).	The gel had a stable appearance (1,458 mm^3).
	M18	Appearance similar to that observed at 6 and 12 months (2,160 mm^3).	Gel infiltrated significantly distally in a fan-shaped manner (1,495 mm^3).
	M24	The shape of the gel remained stable (1,577 mm^3).	The gel almost completely infiltrated distally, still in a fan-shaped manner (1,458 mm^3).
Participant 2		***Stylage®XL-Lido with Lidocaine* (0.55 ml)**	***Stylage®XL without Lidocaine* (0.50 ml)**
	AT	Gel in the form of a papule with smooth convex edges and uniform structure located very deep in pre- and particularly post-aponeurotic spaces and caudally in the intra-muscular region infiltrating the muscle fibers (1,929 mm^3).	Gel was cigar-shape with a uniform structure and smooth convex edges located deep in pre- and post-aponeurotic spaces, but less deeply than on the right, extending in a fan-shaped manner distally infiltrating the muscle fibers to a significant extent (2,096 mm^3).
	M6	Gel still had convex edges and uniform structure extending caudally with an equal spread in pre- and post-aponeurotic spaces infiltrating the muscle fibers. It extended along the tendons and fibers, which connect the coronoid apophysis (2,936 mm^3).	Gel still located deeply but moved further in the post- than pre-aponeurotic space. It lost its convex appearance and appeared less uniform in structure (3,314 mm^3).
	M12	The gel had a stable appearance (3,221 mm^3).	The gel had a stable appearance (3,868 mm^3).
	M18	The gel had a stable appearance (3,647 mm^3).	The gel had a stable appearance (4,369 mm^3).
	M24	The gel had a stable appearance and shape but linear edges (4,266 mm^3).	The gel had a stable appearance (3,953 mm^3).

AT: After treatment; **M6, M12, M18** and **M24:** 6, 12, 18 and 24-month follow-up time points.

MAS® scores from the participant's and experts' evaluations over 24 months there was a change in score "from very severe" to "moderate" and from "severe" to "low" loss of volume after the use of *Stylage® XL* and *XL-Lido* respectively. All evaluators observed slow resorption by comparing the visual appearance in the photographic records, but this resorption was less marked for the *XL- Lido* gel after 24 months. Nevertheless, it is important to take into account the slight difference in the MAS® score at baseline for both sides. For participant 2, there was an improvement in the MAS® score at 24 months compared to baseline based on the participant's assessment. Nonetheless, the improvement based on experts' average score was only achieved for *Stylage® XL-Lido*. These improvements were also demonstrated on the participants' and experts' GAIS scores in both women. However, these were slightly better in the *Stylage® XL-Lido* side for participant 1 only.

Adding lidocaine to gels during manufacture can affect the rheological characteristics of the gel [10]. These variations can possibly lead to a difference in the stability of the gel over time when compared to the same gel without lidocaine [4]. In our study, both gels appeared stable over time. Although there was a perceived reduction in volume between 12 and 18 months, there was no apparent difference between the gels at 24 months, except perhaps in the participant with the most skeletonization (participant 1). Similarly, on MRI, the gels appearance, both for *XL* and *XL-Lido*, did not change between the 6 and the 24-month follow-up periods. Hence, it is plausible that, just as for the Non-Animal Stabilised Hyaluronic Acid (NASHA) technology, the resorption of the gel occurs iso-volumetrically. It is suggested that shear forces could have caused the change in gel shape over the first 6 months. However, it is important to stress that although we have undertaken multiple objective and validated

Table 3: MAS© and GAIS scores as evaluated by participants and experts at the different time point.

			Right temple						Left Temple					
Participant 1	Gel		*Stylage®XL,* (1.0 ml)						*Stylage®XL-Lido* (1.0 ml)					
	Assessor		Participant's score			Average expert' score			Participant's rating			Average expert' rating		
	Scale		MAS	ΔMAS	GAIS	MAS	ΔMAS	GAIS	MAS	ΔMAS	GAIS	MAS	ΔMAS	GAIS
	MAS	BT	4	-	-	3.75	-	-	3	-	-	3.75	-	-
		AT	2	2	3	1.75	1.75	3	1	2	3	2	1.75	3
		M6	2	2	3	2	1.5	2.75	1	2	4	2	1.75	2.5
		M12	2	2	3	2	1.5	2.5	1	2	2	2.25	1.5	2.5
		M18	3	1	2	2.25	1.25	2.5	3	0	3	2	1.75	2.5
		M24	1	3	3	2.5	1.0	2	1	2	3	1.4	2.35	2.5
Participant 2	Gel		*Stylage®XL-Lido* (0.55 ml)						*Stylage®XL* (0.50 ml)					
	Assessor		Participant's score			Average expert' score			Participant's rating			Average expert' rating		
	Scale		MAS score	ΔMAS	GAIS	MAS score	ΔMAS	GAIS	MAS score	ΔMAS	GAIS	MAS score	ΔMAS	GAIS
	MAS	BT	2	-	-	1.75	-		2	-	-	1.25	-	
		AT	1	1	4	0.75	1	2.75 1	1	1	4	0.75	0.5	2.75
		M6	0	2	4	1	0.75	2.75	0	2	4	1	0.25	2.5
		M12	0	2	4	0.75	1	2.5	0	2	4	0.75	0.5	2.5
		M18	0	2	4	0.75	1	2.75	0	2	4	0.75	0.5	2.5
		M24	1	1	4	1.25	0.5	2	1	1	4	1.25	0	2.25

ΔMAS: Points of improvement compared to before treatment; **BT:** Before treatment; **AT:** After treatment; **M6, M12, M18** and **M24:** 6, 12, 18 and 24 month follow-up time points.

Table 4: Evaluation of the efficacy of "IPN-Like" HA gel *Stylage® XL and XL-Lido injections in* the temporal fossa according to the MAS® and GAIS scale by experts.

	Expert		BT		AT		M6		M12		M18		M24	
Participant 1			R	L	R XL	L XL-Lido	R XL	L XL-Lido	R XL	L XL-Lido	R XL	L XL-Lido	R XL	L XL-Lido
	MAS®	1	4	4	2	3	3	2	2	3	2	2	3	2
		2	3	4	2	2	2	2	3	2	3	2	2	1
		3	2	3	0	1	0	2	0	2	0	2	1	2
		4*	4	4	3	2	3	2	3	2	4	2	4	2
Participant 2	GAIS													
		1			3	3	3	2	3	3	3	3	2	2
		2			2	2	2	2	1	1	1	1	1	2
		3			4	3	4	2	4	2	4	2	3	2
		4*			3	4	2	4	2	4	2	4	2	4
Participant 1			R	L	R XL-Lido	L XL	R XL-Lido	L XL	R XL-Lido	L XL	R XL-Lido	L XL	R XL-Lido	L XL
	MAS®	1	2	2	1	1	1	1	1	2	0	1	1	1
		2	1	1	1	1	1	1	0	0	1	1	1	2
		3	2	2	1	1	1	1	1	1	1	1	2	2
		4*	2	0	0	0	0	1	1	0	1	0	1	2
Participant 2	GAIS													
		1			4	4	4	3	3	3	4	3	3	3
		2			1	1	1	1	1	1	1	1	1	1
		3			2	2	2	2	2	2	2	2	1	1
		4*			4	4	4	4	4	4	4	4	3	4

*Physician who performed the injections. *XL*: ***Stylage® XL*** without lidocaine; *XL-Lido*: ***Stylage® XL*** with lidocaine; **R:** Right; **L:** Left; **BT:** Before treatment; **AT:** After treatment; **M6, M12, M18** and **M24**: 6, 12, 18 and 24 month follow-up time points.

subjective measures, these observations involve only 2 participants and such information should be interpreted with caution till further evidence is available.

Conclusion

Adding lidocaine to hyaluronic acid gels, especially when intended for correcting volume loss with deep intramuscular injections close to the bone, is an advantage based on patient reported level of pain perception. There were some variations in the reported scores by patients and experts on the MAS® and GAIS scales at different time-points. However, both types of HA preparations seemed to behave fairly similarly and achieved comparable results. Nevertheless, we observed an advantage with *Stylage® XL-Lido* in that it was more stable over time on the GAIS scale. It would be prudent to confirm our observations in larger studies involving more patients, multiple centers and longer follow-up duration before drawing final conclusions.

Acknowledgement

The authors would like to sincerely thank the two study participants for their involvement. We also want to thank Dr O Jordan, MD-PhD, for his expert observation about the shear forces. Dr D Sarazin, Institut Viollier, Geneva (Switzerland), for their help with researching the anatomy of the periosteum in the temporal fossa, Mrs Maria Ferros, secretary to P Micheels, for her valuable work, laboratoire Vivacy-Archamps, France for supplying the HA gels used for this study and The radiology institute MedImage, Geneva, Switzerland, for allowing us to use their equipment. We would also like to acknowledge Superviseme LTD-medical writing services-(http://www.superviseme.eu) for their support with the medical writing and editing of the manuscript, which was funded by LABORATOIRES VIVACY.

Declarations of Interest

The syringes were supplied by the Laboratoire Vivacy, Archamps, France. Dr S Besse was remunerated for the radiology work she performed. The other authors declared no conflict of interest, having received no financial compensation in return for the work carried out. Dr P Micheels is a consultant and/or trainer for Allergan, IBSA, Galderma Q-Med Switzerland, KioMed, Kylane, Merz, Sinclair, Teoxane and Vivacy. Dr J Vandeputte is a consultant and trainer for Merz and Advanced Aesthetic Technologies.

References

1. Olenius M (1998) The first clinical study using a new biodegradable implant for the treatment of lips, wrinkles, and folds. Aesthetic Plast Surg 22: 97-101.
2. Duranti F, Salti G, Bovani B, Calandra M, Rosati ML (1998) Injectable hyaluronic acid gel for soft tissue augmentation: A clinical and histological study. Dermatologic Surg 24: 1317-1325.
3. Wahl G (2008) European evaluation of a new hyaluronic acid filler incorporating lidocaine. J Cosmet Dermatol 7: 298-303.
4. Prager W, Micheels P (2015) A prospective, comparative survey to investigate practitioners' satisfaction with a cohesive, polydensified-matrix®, hyaluronic acid- based filler gel with and without lidocaine for the treatment of facial wrinkles. J Cosmet Dermatol 14: 124-129.
5. Beaunis HÉ, Bouchard A (2015) Nouveaux éléments d'anatomie descriptive et d'embryologie. (5th edition) Paris: J-B Baillière.
6. Masson A, Keribin P, Vacher C, Benateau H, Veyssiere A, et al. (2018) Étude Anatomique D'Insertions Tendineuses Exocrâniennes Du Muscle Temporal Au- Dessus De La Crête Sphéno-Temporale. Morphologie 102: 193.
7. Idone F, Bolletta E, Piedimonte A, Paternostro F (2020) Temporal Fossa Atrophy in Aesthetic Medicine: Anatomy, Classification, and Treatment. Plast Reconstr Surg Glob Open 8: e3169.
8. Bajpai H, Saikrishna D (2011) The Versatility of Temporalis Myofascial Flap in Maxillo- Facial Reconstruction: A Clinical Study. J Maxillofac Oral Surg 10: 25-31.
9. Becker M, Balagué N, Montet X, Calmy A, Salomon D, et al. (2015) Hyaluronic acid filler in HIV-associated facial lipoatrophy: Evaluation of tissue distribution and morphology with MRI. Dermatology 230: 367-374.
10. Micheels P, Obamba M (2018) Rheological properties of several hyaluronic acid-based gels: A comparative study. J Drugs Dermatology 17: 948-954.
11. Sundaram H, Rohrich RJ, Liew S, Sattler G, Talarico S, et al. (2015) Cohesivity of hyaluronic acid fillers: Development and clinical implications of a novel assay, pilot validation with a five-point grading scale, and evaluation of six US food and drug administration-approved fillers. Plast Reconstr Surg 136: 678-686.
12. Flynn TC, Sarazin D, Bezzola A, Terrani C, Micheels P (2011) Comparative histology of intradermal implantation of mono and biphasic hyaluronic acid fillers. Dermatologic Surg 37: 637-643.
13. Micheels P, Sarazin D, Tran C, Salomon D (2016) Effect of different crosslinking technologies on hyaluronic acid behavior: A visual and microscopic study of seven hyaluronic acid gels. J Drugs Dermatology 15: 600-606.
14. Carruthers J, Jones D, Hardas B, Murphy DK, Donofrio L, et al. (2016) Development and validation of a photonumeric scale for evaluation of volume deficit of the temple. Dermatologic Surg 42: S203-S210.
15. Gupta V, Sharma VK (2019) Skin typing: Fitzpatrick grading and others. Clin Dermatol 37: 430-436.
16. Brannon HL How the Glogau Classification System Measures Photoaging nd.