



ORIGINAL CONTRIBUTION



WILEY

Customized lip enhancement for clinical different lip features: An observational study

Michela Zazzaron MD

Medicina Estetica Zazzaron, Treviso, Italy

Correspondence

Michela Zazzaron, Zazzaron Aesthetic Medicine Ambulatory, Via Fusana 7, Roncade, Treviso, Italy.
Email: michela@medicinaesteticazazzaron.it

Abstract

Background: The request for lip improvement treatments with injectable hyaluronic acid (HA) is increasing. However, as the patient's needs can be extremely different, it is unconceivable to use the same technique/product for clinical different lips to grant customized results.

Aims: To provide a specific treatment approach for clinically different lips based on the Author's clinical experience.

Patients/Methods: Patients belonged to four clinical groups: young lips requiring volume enhancement or a reshaping intervention, and senescent lips requiring rejuvenation or a rebuild intervention. At first visit T0, subjects underwent a pretreatment evaluation and the investigator performed an individual treatment based upon patient's esthetic goals and lip's baseline features. Lip fullness was assessed by the investigator using a Medicis Lip Fullness Scale (MLFS) at first visit (T0) and at 2 weeks (T1). Subjects and investigator answered to the Global Aesthetic Improvement Scale (GAIS) at 2 weeks T1 and at 12 weeks (T2). A photographic evaluation was undertaken at T0 and T2.

Results: Only, in the two groups requiring volumization there was 1 grade of improvement in the MLFS (young lips—volume and senescent lips—rebuild). Nonetheless, the performed combination of techniques/products was overall very satisfactory: 80% of the subjects reported a much improved/very much improved outcome in the GAIS, and the same was reported by the investigator in 90% of the subjects. A weak positive correlation was found between MLFS responses and subject's GAIS at T1 in all groups.

Conclusions: This customized treatment approach, consisting in choosing the right gel technology injected in minimum quantities with the right technique, ensures a harmonic result avoiding aberrations and standardizations.

KEYWORDS

customized treatment, injectable hyaluronic acid, lip enhancement

1 | INTRODUCTION

The last two decades have seen a growing trend on the request for noninvasive esthetic medicine treatments.¹ This phenomenon is

probably due to a widespread social need and/or desire for beauty that has reached both sexes of nearly every age, group, and ethnicity.

Inappropriately, esthetic treatments are often proposed as a “one-size-fits-all” solution. However, no treatment is effective

for everyone, and individual characteristics must be carefully assessed in order to achieve a natural look with minimal risk for adverse events. In particular, as lips are a central and outlining feature of the face,² a tailored approach able to match lip baseline features and patient requests (eg, volume, shape, aging modification) should be crucial to choose the most suitable treatment, both in terms of injection technique and injectable product.

In this attempt to achieve a personalized outcome, one of the greatest challenges for surgeons is the demand, besides volume augmentation, of more sophisticated interventions such as correction of labial asymmetry, changing of lip shape, and rejuvenation of oral and perioral region.

Hyaluronic acid (HA), a glycosaminoglycan-based polymer, is one of the principal molecules on the market used for nonpermanent dermal treatments.^{3,4} HA has a well-recognized role in skin support and turgor given to its viscoelasticity that enables it to attract water into its own matrix within the connective tissue.³⁻⁶ In general, HA-based injectables differ in terms of the gel's characteristic that affects the product longevity and viscoelasticity, in particular concentration, degree of cross-linking, and particle sizing.⁵⁻⁷

The products used in this study were NASHA[®] (Non Animal Stabilised HA), Restylane[®] Skinbooster Vital, and Restylane[®] Lidocaine (Galderma, Uppsala, Sweden) and OBT[®] (Optimal balance technology) and Restylane[®] Kysse (Galderma, Uppsala, Sweden), which are all compatible to fine gauge needles (29 and 30 G) and to the superficial injection required for lip enhancement procedures.⁸ These HA gels, based on patented technologies, share the HA concentration (20 mg/mL) but vary in the degree of cross-linking and in particle size, resulting in differ adaptable solutions able to address individual needs and are among the most widely acknowledged products for nonpermanent soft tissue treatments.^{9,10}

Up to now, to the best of our knowledge, there is no available treatment algorithm that takes into account the anatomical and clinical specificity of different lips, the patient's esthetic needs, and the necessity to avoid esthetic aberrations. This study reported by the author clinical experience and the effects of specific combinations of injection techniques and HA-based injectables for lip enhancement assessed in order to attain an individualized treatment approach and a harmonic result.

2 | MATERIALS AND METHODS

This is a descriptive, retrospective, observational, monocentric study of patients attending the Zazzaron Aesthetic Medicine ambulatory (Treviso, Italy) for a lip improvement procedure with HA-based products between 2016 and 2017. Among all treated subjects, the electronic medical database was reviewed for those patients aged between 18 and 82 years old, in a good health and belonging to four anatomical and clinical groups, each group including 10 patients:

1. Young lips requiring volume enhancement;
2. Young lips requiring a reshaping intervention;

3. Senescent lips requiring rejuvenation;
4. Senescent lips requiring a rebuild intervention.

Senescent lips were defined in the presence of one or all of these conditions: thin and dehydrated lips, loss of Cupid's bow, flattened philtral columns, loss of projection of the lips, commissures downturned, and/or loss of definition and roughness of vermilion borders.^{7,11} All those lips not presenting these features were classified as young. Before including patients in the study, an informed consent form was obtained to collect data and photographs. Exclusion criteria included incompatibility to treatment with HA.

Each subject attended three visits at the investigation site. At the first visit (T0), the subject underwent a pretreatment evaluation, which included assessment of the patient's face and discussion on his/her requests, explanation of the choice of a technique and a HA-based product, and evaluation of lip fullness using a 5-point Medicis Lip Fullness Scale (MLFS) for both the upper and lower lip, as shown in Table 1. After makeup removal, the investigator took frontal, lateral, and three-quarter projection photographs, and applied topical anesthesia (70 mg/g lidocaine + 70 mg/g tetracaine cream) for 20 minutes on the region to be treated; however, the HA gels injected contain Lidocaine as well.

After removal of anesthetic cream and disinfection of the area, the investigator performed the inoculation of a Restylane[®] filler with a 29 or 30 G needle, in the submucosae layer with a linear backward technique or a bolus technique.

For each group, investigator injected specific lip areas choosing OBT or NASHA gel technology according to the esthetic outcome to achieve and to the quality of the skin. Concerning rheological features, investigator chose mostly NASHA gel for lip reshaping intervention (asymmetries, very aged lips, anatomical disharmonies), whereas for a simple volume effect, OBT gel was selected. At the end of the treatment, the investigator performed a light massage and applied ice and antibiotic ointment.

The side effects reported were in line with usual HA treatments (swelling from mild to moderate and occasional bruising).

The photographic documentation was acquired in the immediate post-treatment, with a Nikon D 3300 camera D-SLR, 24.2 megapixel, zoom AF-P DX NIKKOR 18-55mm F/3.5-5.6G.

TABLE 1 Scales used to verify the effectiveness of the treatment

MFLS		GAIS	
5	Very full	3	Very much improved
4	Full	2	Much improved
3	Medium	1	Improved
2	Thin	0	No change
1	Very thin	-1	Worse
		-2	Much worse
		-3	Very much worse

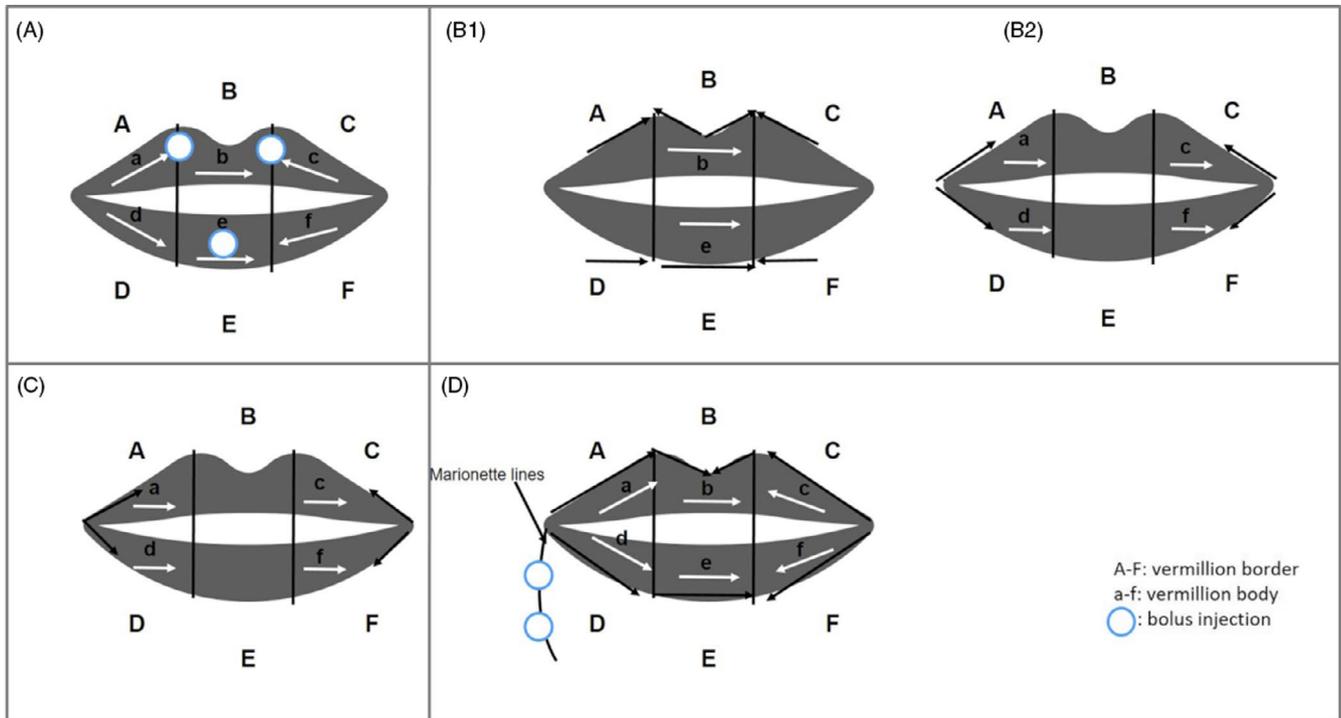


FIGURE 1 Injectable techniques (A) Young lips—volume (B1, B2) Young lips—reshaping (C) Senescent lips—rejuvenate (D) Senescent lips—rebuild

The patient remained under observation for 20 minutes. At 2 weeks (T1), MLFS was assessed by the investigator. Moreover, subjects and investigator assessed the level of global satisfaction using a 7-point Global Aesthetic Improvement Scale (GAIS), at T1, and at (T2) (Table 1). Finally, at T2, photographic evaluation was undertaken.

According to his experience, the investigator chose a specific injection technique according to baseline lip features and the esthetic goal to achieve. Investigator performed as follows:

1. Young lips requiring volume enhancement: Restylane® Kysse (0.5-1 mL) was injected in the vermilion body (a + b + c and d + e + f areas) with a linear backward technique; a bolus filler injection was performed from the external mucosa just at the limit of the a/b area and the b/c area, and in the e area. Optional filler injection of the border of the vermilion was performed (Figure 1A).

Restylane Kysse is suitable for volumization because of its moderate flexibility and firmness. As a matter of fact, lips are a very dynamic anatomical area, subject to stretch and movements; thus, it is important to use a resistant but soft gel that integrates itself smoothly in the tissue and that can resist to the stretching as well.

2. Young lips requiring a reshaping intervention: Two different combinations of technique/injectable gel were performed. Restylane® Lidocaine (0.5-1 mL) was injected in order to obtain a narrowing and remodeling effect. In the upper lip, the product was injected in the vermilion borders (A + B + C areas) and

in the central vermilion body (b area) with a linear backward technique; in the lower lip, the gel was injected in the vermilion borders (D + E + F areas) and in the central vermilion body (e area) with the same linear backward technique (Figure 1B1). On the other hand, to achieve an enlargement and plumping effect, Restylane® Kysse (0.5-1 mL) was injected with a linear backward technique in external commissures of upper and lower lip. Moreover, in the upper lip the external vermilion body was injected (a and c areas) with a linear backward technique, and the same specular technique was performed in the lower lip (d and f areas; Figure 1B2).

Nasha Restylane technology comes out as a firm gel, very resistant to deformation, and able to create support into the tissue; it is, therefore, suitable for a real reshaping of the anatomical area, even in very thick skin.

3. Senescent lips requiring rejuvenation: Restylane® Kysse or Restylane® Lidocaine (0.5 mL) was alternatively injected depending on the desired esthetic outcome. The first product was used to rejuvenate lips by adding volume and contour, while the latter was used to restore the original lip shape, lost with the aging process. Only one technique was applied. In the upper lip, both external commissures (vermillion borders A + C and vermilion body a + c areas) were injected with a linear backward technique, and in the lower lip, both external commissures (vermillion borders D + F and vermilion body d + f area) were injected with linear backward technique (Figure 1C). HA was not injected in the central portion of vermilion because it is possible to obtain a harmonious eversion

TABLE 2 Demographic parameters within clinical groups

	Young lips volume	Young lips reshaping	Senescent lips rejuvenate	Senescent lips rebuild
Age (±SD)	32.4 (±8.67)	34.4 (±7.98)	55.8 (±5.49)	56.7 (±11.30)
Sex, n (%)				
Females	10 (100%)	10 (100%)	8 (80%)	10 (100%)
Males	0	0	2 (20%)	0

of the central part of the lips simply injecting the commissures first, avoiding a volumizing effect.

According to the skin quality in this group, we chose OBT technology (Restylane Kysse) in very thin and anelastic skin, whereas NASHA was preferred for thicker skin.

4. Senescent lips requiring a rebuild intervention: Restylane® Skinbooster (3.2 mL as the average overall final amount, performed in 3 sessions) was always injected to improve skin quality in perioral area as well as to treat fine lines and wrinkles.

We applied Restylane Skinbooster to rejuvenate perioral areas (bar code, lateral canthus area, perioral fine lines, and wrinkles) to improve the overall skin quality. We usually injected 1 mL per session, in line with the 2018 consensus on NASHA technology as a skin quality booster.¹²

Restylane Skinbooster was coupled with 0.5-1 mL of Restylane Kysse or Restylane® Lidocaine, injected into the lips to treat the

mucosal area. The redefinition of the vermilion border was always performed on the external commissures (vermillion borders A + B + C and D + E + F) both on the upper and on the lower lip. Moreover, the vermilion body (a + b + c and d + e + f areas) was injected with a linear backward technique both on the upper and on the lower lip. Bolus injections from external mucosa just at the limit of the vermilion body a/b, b/c, d/e, and e/f areas were added. Concerning marionette lines, they were injected with a bolus injection (Figure 1D) when necessary.

2.1 | Statistical analysis

Mean and standard deviation of subject's age was calculated within each group. Paired T test was used to compare the MLFS response rates and differences between GAIS scales, and a P-value < .05 was considered to be statistically significant. Patients were defined as “responders” with at least 1 grade of improvement on the MLFS assessed by the investigator at T1; these rates were calculated for

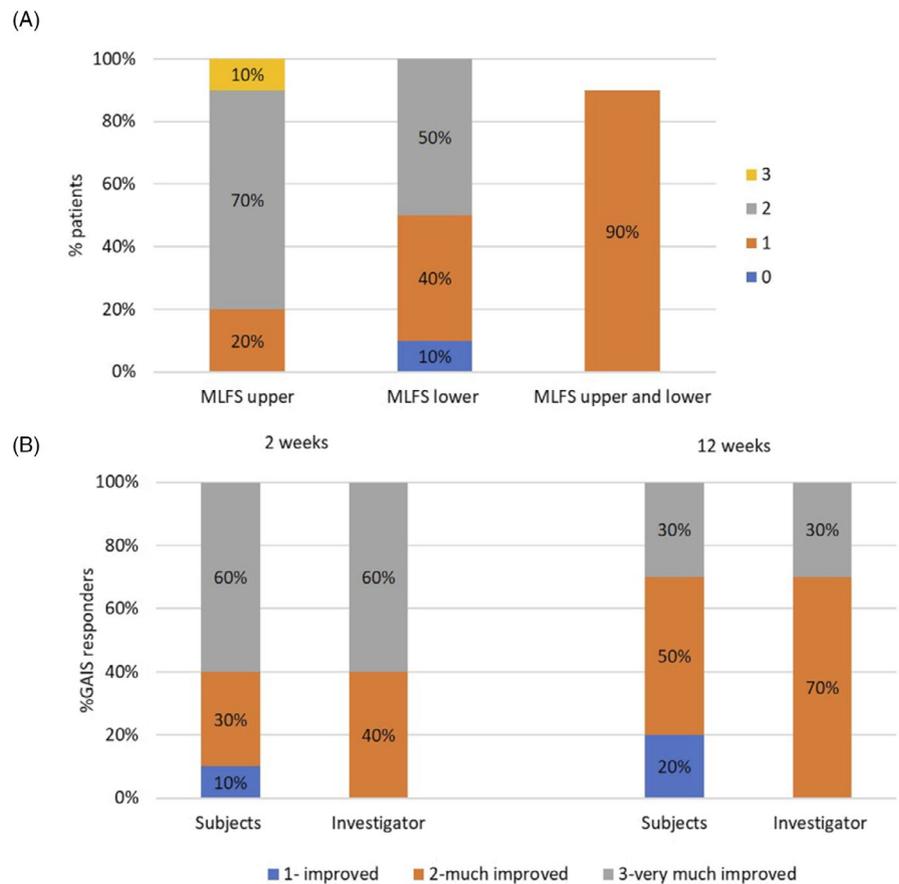


FIGURE 2 Young lips—volume (A) Percentage of responders with 0, 1, 2, and 3 grades of improvement in the MLFS in upper, lower, and both lips by the investigator. (B) Proportions of subjects with improvement in GAIS in both upper and lower lips assessed by the investigator and the subjects

upper and lower lips for all groups. The statistical differences among GAIS scales were assessed for subjects, investigator, and between subjects and investigator at T1 and T2. Moreover, the correlation between MLFS and GAIS scores was determined for all groups using the Spearman rank. Database, results table and statistical analysis is available at Supplementary Information .

3 | RESULTS

A total of 40 subjects (38 females, 2 males) were included in the study. Ten subjects for each group: (i) young lips—volume; (ii) young lips—reshaping; (iii) senescent lips—rejuvenate; (iv) senescent lips—rebuild. Demographic parameters for each group are described in Table 2.

3.1 | Young lips—volume

100% of subjects showed at T1 at least 1 grade of improvement on the MLFS for upper and lower lip based on the investigator assessment. No significant difference between upper and lower lips, according to the MLFS response, was found ($P = .09$). The MLFS responders of combined upper/lower lip at T1 were 90% (Figure 2A). A representative photo of before and after treatment at both T1 and T2 is shown in Figure 3A and B. Esthetic appearance (GAIS) results according to the patients and the investigator are shown in Figure 2B. All patients rated themselves at least as “improved” at T1 and T2. The investigator also rated 100% of subjects at least as “improved” at T1 and T2. A significant difference between subjects GAIS at T1 and T2 was found ($P = .03$). No statistically significant difference was found between investigator's GAIS at T1 and T2, and between GAIS of subjects and investigator at any time point ($P = .34$

for T1 and $P = .167$ for T2) (Figure 2B). The correlation analysis between patients' GAIS at T1 and the cumulative mean of MLFS response for upper and lower lips showed a weak positive correlation (data not shown).

3.2 | Young lips—reshaping

According to the investigator, 1 grade of improvement on MLFS was achieved in 40% of the subjects for the upper lip and in 10% of the subjects for the lower lip. The difference between upper and lower lip MLFS response was not significant ($P = .08$). The MLFS responders of combined upper/lower lip at T1 were 10% (Figure 4A) A representative photograph of before and after treatment at T1 and T2 is shown in Figure 3C and D. Results of GAIS scoring according to both patients and investigator are shown in Figure 4B. GAIS of 100% of the subjects was at least “much improved” at T1 and T2 according to both opinions. No statistically significant differences were found between subject's GAIS at T1 and T2 ($P = .34$), investigator's GAIS ($P = .17$), and between subjects and investigator GAIS ($P = 1.00$ for T1 and $P = .34$ for T2). A weak positive correlation was found between the cumulative mean of MLFS response for upper and lower lip and subject's GAIS at T1 (data not shown).

3.3 | Senescent lips—rejuvenate

Based on the investigator's assessment, at T1, 1 grade of improvement on MLFS was achieved in 40% of the subjects for the upper lip, while no patients showed this improvement for the lower lip (Figure 5A). The difference between upper and lower lip on MLFS response rate was statistically significant ($P = .03$). A representative photograph of before and after treatment at T1 and T2 is

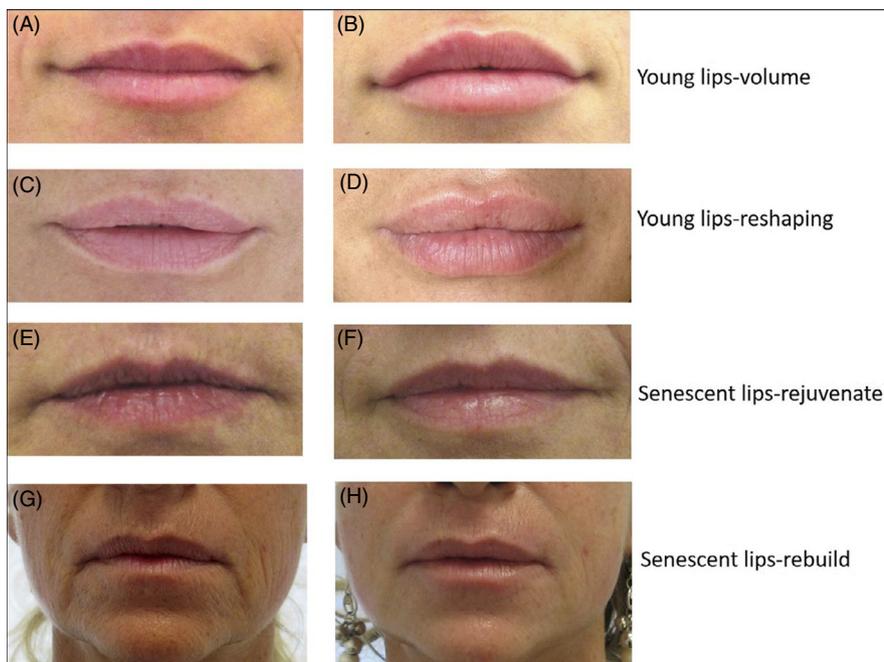
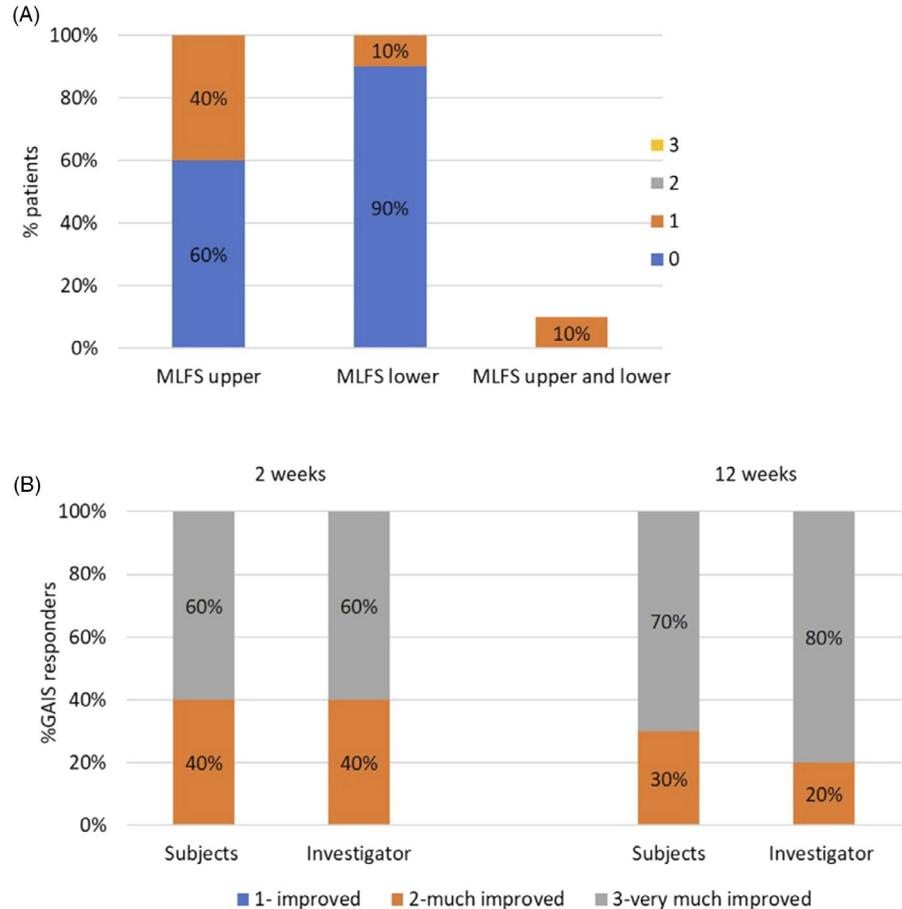


FIGURE 3 Representative lips of patients (A, C, E, G) before treatment and (B, D, F, H) post-treatment

FIGURE 4 Young lips—reshaping (A) Percentage of responders with 0, 1, 2, and 3 grades of improvement in MLFS in upper, lower, and both lips by the investigator. (B) Proportions of subjects with improvement in GAIS in both upper and lower lips assessed by the investigator and the subjects



shown in Figure 3E and F. Results of subject's and investigator's GAIS scoring are shown in Figure 5B. All subjects rated themselves at least as "much improved" at T1 and T2, also the investigator rated 100% of patients at least as "much improved" at any time point. No statistical differences were found between subjects GAIS at T1 and T2 ($P = .08$), between investigator GAIS at T1 and T2 ($P = .16$), and between subjects and investigator GAIS at any time point ($P = .34$ for T1). Statistical significance was not calculable at T2 because subjects and investigator GAIS score were identical. The correlation at T1 of subjects GAIS was weak positive if related to the MLFS upper lip response, while a correlation with MLFS of lower lip was not calculable because data set had values zero.

3.4 | Senescent lips—rebuild

By the investigator's assessment, 90% of treated subjects achieved 1 grade of improvement on MLFS for upper lip and at least 1 grade of improvement for lower lip (20% of them had 2 grades) as shown in Figure 6A. No significant difference between upper and lower MLFS response was found ($P = .34$). The MLFS responders of combined upper/lower lip at T1 were 80% (Figure 6A). A representative photograph of before and after treatment at T1 and T2 is shown in Figure 3G and H. Results of GAIS scoring according to the patients and the investigator are shown in Figure 5B. 100% of the subjects

considered themselves at least as "improved" at T1 and T2, according to the investigator all patients were at least "improved" at both time points (Figure 6B). A significant difference between subject's GAIS at T1 and T2 was found ($P = .01$). Any statistical differences were found between investigator's GAIS at T1 and T2 (P -value was not calculable because scores were identical) and between subjects and investigator GAIS at any time point ($P = .10$ for T1 and $P = .59$ for T2). A weak positive correlation was found between the cumulative mean of MLFS response for upper and lower lip and subject's GAIS at T1 (data not shown).

4 | DISCUSSIONS

The evolution of request for lips rejuvenation and reshaping in esthetical medicine implies the necessity to find a new treatment approach of this region. Thus, in order to satisfy patient demands and avoid standard or disharmonious result, we need to match patient clinical and anatomical baseline features and specific injection techniques/products.

The clearest finding, which emerges from this analysis, is that considering all the groups, the HA-based injectables here investigated were very well accepted by both subjects and physicians, with 80% of the subjects reporting a "much improved" or "very much improved" outcome in their lips after the first injection, and the

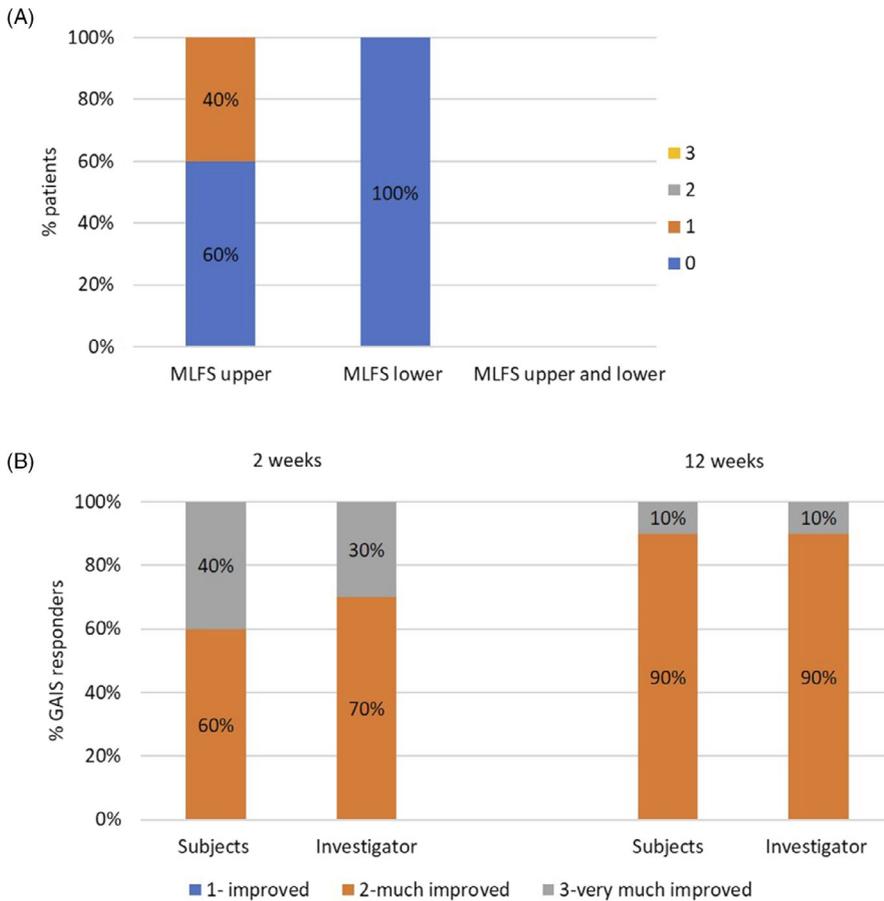


FIGURE 5 Senescent lips—rejuvenate (A) Percentage of responders with 0, 1, 2, 3 grades of improvement MLFS in upper, lower, and both lips by the investigator. (B) Proportions of subjects with improvement in GAIS in both upper and lower lips assessed by the investigator and the subjects

physicians reporting a “much improved” or “very much improved” outcome in 90% of the subjects. It is important to underline that in this study, lip classification did not take into account age, but rather clinical and anatomical conditions. This is a proof of how smoke, sun exposure, and other factors can accelerate the aging of the oral and perioral region, that is particularly prone to damage and photo-aging even at a young age.¹¹

Concerning “young lips—volume” group, the performed combination of techniques and HA-based gels was generally very satisfactory. In most cases, the volumizing effect was mild/moderate with a greater volumetric augmentation in the upper lip (70% of cases had an increase of 2 points in the MLFS scale). This finding confirms and, in some way, endorses the contemporary canons of beauty in terms of lips. In fact, these results are in accord with a recent study and set out to clarify lips most attractive features and gender-related differences: A full upper lip seems to be a central feature of both feminine and masculine attractiveness.¹³

Despite being the lips an area subject to high dynamic stretching, another interesting finding is that the esthetic result in the “young lips—volume” group persisted over time, with 70% of the subjects reporting a “much improved” or “very much improved” outcome at 12 weeks, and the physicians reporting a “much improved” or “very much improved” outcome in 90% of the subjects. These data are in line with other studies describing, evident lip improvements up to 6 months after treatment, using the same HA gel.¹⁴

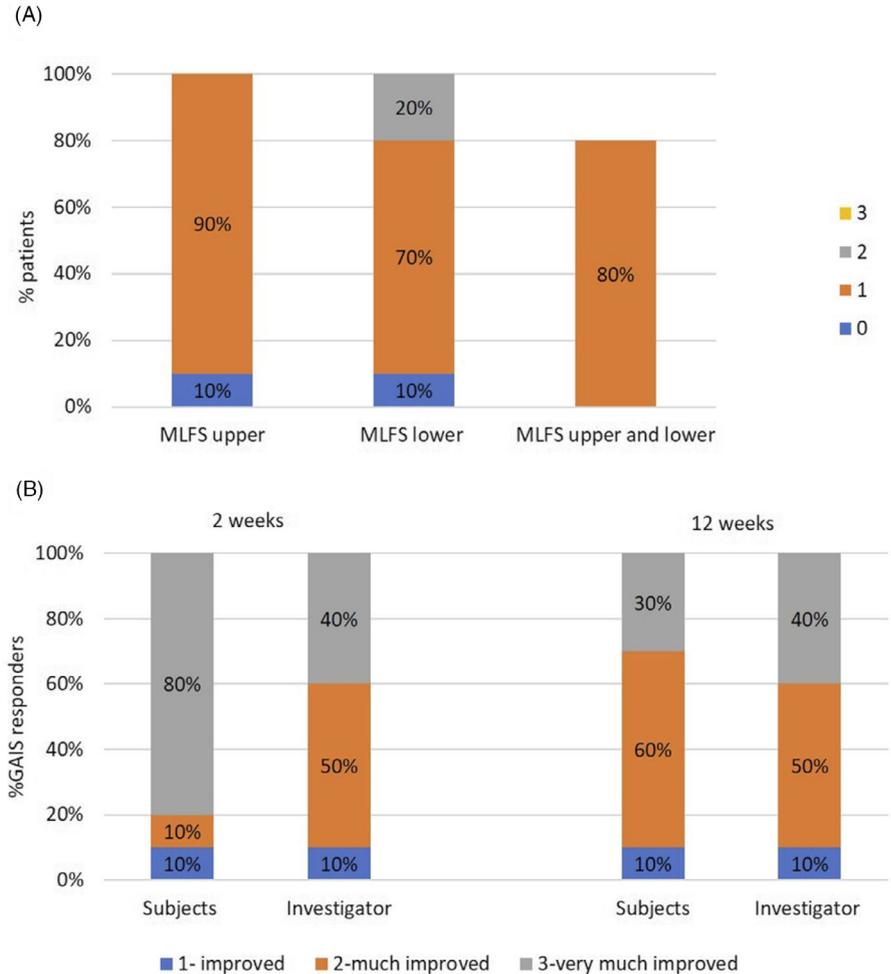
However, it should be highlighted how the perception of the health practitioner and the patient are slightly different concerning the long-lasting volumizing result; the patient usually feels a stabilization of the lip volume the first weeks after the treatment.

In terms of satisfaction, also the “young lips—reshaping” patients considered the esthetic result fully adhering to their expectations. It is important to underline that, among this group, in most cases, it was not necessary to perform a volumetric increase to reshape lips? These data imply, once again, that a customized treatment is sufficient to deliver an optimal final esthetic outcome.

The third query in this research was about the “senescent lips—rejuvenate” group treatment algorithm. The results of the study confirm that also in these patients the lip enhancement effect with the applied technique/products was satisfactory and maintained over time. In the case of senescent lips, these outcomes are probably the consequence of the HA-based injectable physiochemical properties together with the choice of the dose applied by the investigator (0.5 mL average). This very specific combination was, indeed, sufficient to qualitatively restore the skin and the mucosa, overall increasing its hydration, elasticity, and firmness.

Several studies have correlated a progressive and continuous improvement of the skin quality to the ability of NASHA[®] formulations to stimulate fibroblasts in the reticular dermis through a mechanical stretching mechanism.¹⁵⁻¹⁷ In fact, these stimulated fibroblasts, in turns, seem to induce the synthesis of type-I collagen and procollagen.¹⁵⁻¹⁷

FIGURE 6 Senescent lips—rebuild
(A) Percentage of responders with 0, 1, 2, and 3 grades of improvement in the MLFS in upper, lower, and both lips by the investigator. (B) Proportions of subjects with improvement in GAIS in both upper and lower lips assessed by the investigator and the subjects



Also, in the “senescent lips—rejuvenate” group the treatment approach seemed to be suitable and, as in the “young lips—reshaping” one, there is no correlation between a volumetric increase and the achievement of the esthetic goal.

Thus, it seems possible to treat lips with injectables not aiming for volumetric increase, and furthermore, this approach can fully satisfy patient’s needs preventing undesired lip volumization, which is the effect that more and more patients are afraid of and could discourage to undergo an HA treatment.

Finally, an optimal satisfaction was obtained also in the “senescent lips rebuild” group. It is clear that the complete reconstruction of the labial or peri labial area required an expansion of the tissue volume and a greater amount of gel injected.

These data show that applying a treatment algorithm consisting of a specific pattern of injection and a combination of HA-based products to produce this expansion was sufficient to guarantee a substantial patient and health practitioner agreement. Moreover, these results seem to be consistent with other studies which found that the same HA-based products are able to effectively improve plumpness and the appearance of fine superficial wrinkling.^{6,14}

This study also emphasizes the possibility of using minimum quantities of product to achieve a progressive pleasant rejuvenation effect, stable at month 3, as highlighted by the GAIS scores.

Furthermore, we could expect the tissue will benefit from a bio-stimulation as the time goes by, as demonstrated by several studies that highlight the power to regulate triggering factors of the collagen synthesis for weeks after the treatment.^{14,15,18}

There were several limitations of this descriptive study. A potential bias may be subtle variations in injection technique and the lack of precise effect definitions (eg, volumizing, reshaping). However, a subjective (patient and investigator) outcome evaluation was considered to be the most appropriate approach, considering the aim of the study. Another limitation of the study could be the relatively restricted follow-up period; however, the long-term efficacy and safety of all the used product have previously been investigated and are not the aim of this study.^{14,18,19}

5 | CONCLUSIONS

This study was undertaken to evaluate the effects of a diversified use of available HA-based gels, in terms of specific rejuvenation results, reshaping, and volumization in a real-world setting and propose a new classification of the 4 clinical lips categories, to which apply a specific treatment algorithm.

One of the more significant findings, which emerged from this study, is that the treatment requests are evolving toward a search

for a harmonic effect that does not necessarily require volumizing. Thus, it is crucial to know when and how to use specific injection techniques/products to achieve a natural effect avoiding volumization, if not desired.

This study also emphasizes the possibility of using minimum quantities of product to achieve a progressive and stable rejuvenation effect, also in the long term. However, this finding is closely related to the product used which have demonstrated to have a sustained effect due to the improved degradation resistance and their power to regulate triggering factors of collagen synthesis for weeks after the treatment.^{14,15,19}

In conclusion, the findings of this small, yet original, study have a number of practical implications and underline how an individualized treatment approach consisting in choosing the right Ha gel, injected in minimum quantities with the right technique, is crucial to obtain a natural and harmonic result.

ACKNOWLEDGMENTS

Medical writing support from *sciencED—medical communication* was funded by Dr Zazzaron.

ORCID

Michela Zazzaron  <https://orcid.org/0000-0003-0336-5059>

REFERENCES

1. American Society for Dermatologic Surgery. 2013 survey on dermatologic procedures. https://www.asds.net/_Media.aspx?xml:id=7744 Accessed on November 19, 2017.
2. Baudouin JY, Tiberghien G. Symmetry, averageness, and feature size in the facial attractiveness of women. *Acta Psychol*. 2004;117:313-332.
3. Salwowska NM, Bebenek KA, Źądło DA, Wcisło-Dziadecka DL. Physiochemical properties and application of hyaluronic acid: a systematic review. *J Cosmet Dermatol*. 2016;15:520-526.
4. Sundaram H, Cassuto D. Plast Biophysical characteristics of hyaluronic acid soft-tissue fillers and their relevance to aesthetic applications. *Reconstr Surg*. 2013;132:5S-21S.
5. Stocks D, Sundaram H, Michaels J, Durrani MJ, Wortzman MS, Nelson DB. Rheological evaluation of the physical properties of hyaluronic acid dermal fillers. *J Drugs Dermatol*. 2011;10:974-980.
6. Bertucci V, Lynde CB. Current Concepts in the Use of Small-Particle Hyaluronic Acid. *Plast Reconstr Surg*. 2015;136:132S.
7. Rohrich RJ, Ghavami A, Crosby MA. The role of hyaluronic acid fillers (Restylane) in facial cosmetic surgery: review and technical considerations. *Plast Reconstr Surg*. 2007;120:41S-54S.

8. Olenius M. The first clinical study using a new biodegradable implant for the treatment of lips, wrinkles, and folds. *Aesthetic Plast Surg*. 1998;22(2):97-101.
9. Glogau RG, Bank D, Brandt F, et al. A randomized, evaluator-blinded, controlled study of the effectiveness and safety of small gel particle hyaluronic acid for lip augmentation. *Dermatol Surg*. 2012;38:1180-1192.
10. Cohen JL, Dayan SH, Brandt FS, et al. Systematic review of clinical trials of small- and large-gel-particle hyaluronic acid injectable fillers for aesthetic soft tissue augmentation. *Dermatol Surg*. 2013;39:205-231.
11. Iblher N, Stark GB, Penna V. The aging perioral region - Do we really know what is happening? *J Nutr Health Aging*. 2012;16(6):581-585.
12. Belmontesi M, De Angelis F, Di Gregorio C, et al. Injectable non-animal stabilized hyaluronic acid as a skin quality booster: an expert panel consensus. *J Drugs Dermatol*. 2018;17(1):83-88.
13. Penna V, Fricke A, Iblher N, Eisenhardt SU, Stark GB. The attractive lip: A photomorphometric analysis. *J Plast Reconstr Aesthet Surg*. 2015;68(7):920-929.
14. Beer K, Glogau RG, Dover JS, et al. A randomized, evaluator-blinded, controlled study of effectiveness and safety of small particle hyaluronic acid plus lidocaine for lip augmentation and perioral rhytides. *Dermatol Surg*. 2015;41:S127-S136.
15. Wang F, Garza LA, Kang S, et al. *In vivo* stimulation of de novo collagen production caused by cross-linked hyaluronic acid dermal filler injections in photo damaged human skin. *Arch Dermatol*. 2007;143:155-163.
16. Landau M, Fagien S. Science of hyaluronic acid beyond filling: fibroblasts and their response to the extracellular matrix. *Plast Reconstr Surg*. 2015;136:188S-195S.
17. Streker M, Reuther T, Krueger N, Kerscher M. Stabilized hyaluronic acid-based gel of non-animal origin for skin rejuvenation: face, hand, and décolletage. *J Drugs Dermatol*. 2013;12:990-994.
18. Quan T, Wang F, Shao Y, et al. Enhancing structural support of the dermal microenvironment activates fibroblasts, endothelial cells, and keratinocytes in aged human skin in vivo. *J Invest Dermatol*. 2013;133(3):658-667.
19. Kerscher M, Bayrhammer J, Reuther T. Rejuvenating influence of a stabilized hyaluronic acid-based gel of nonanimal origin on facial skin aging. *Dermatol Surg*. 2008;34:720-726.

SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of the article.

How to cite this article: Zazzaron M. Customized lip enhancement for clinical different lip features: An observational study. *J Cosmet Dermatol*. 2020;19:38–46. <https://doi.org/10.1111/jocd.13170>