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Volumizing effect of a new hyaluronic acid sub-dermal facial filler: A retrospective analysis based on 102 cases

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Abstract
Introduction: Many signs of aging are due to the loss of subcutaneous fat. Dermal fillers are non-surgical cosmetic treatments used to restore facial volume. Voluma® is a new hyaluronic acid sub-dermal facial filler. The objective of this study was to assess its effectiveness in maintaining increased volume for up to 18 months post-treatment and its safety. *Methods*: Retrospective record analysis was made for 102 patients (93 females, nine males; mean age: 51.27 years) who received Voluma injected into the midface. All patients were assessed at baseline and at 1 month and 6–18 months post-injection. *Results*: Investigator Global Aesthetic Improvement assessment after 1 month and 6–18 months showed that most patients were 'much' or 'very much' improved. Investigator volume loss assessment confirmed that most patients were either stage 1 or 2 (normal or slight ptosis) 1 month post-treatment, which was maintained at 6–18 months. Patient efficacy assessment was 'very good' or 'good' in most cases. *Conclusions*: Voluma provides aesthetic improvements according to investigator and patient assessment for up to 18 months post-treatment. Combination treatment comprising facial fillers and botulinum neurotoxin can enhance treatment benefits. Further methodologically rigorous studies are required to establish the performance of Voluma alone and in combination.

Key words: *Hyaluronic acid, Juvéderm Voluma®, midface, sub-dermal facial filler, tridimensional facial rejuvenation (3D), Voluma®*

Introduction

The effects of aging

The facial stigmas of the aging process are caused by a combination of internal (e.g. aging and genetic) and external factors (e.g. exposure to sun and pollution). Together, they result in the diminished production of collagen, which is the main supporting protein of the skin, as well as a breakdown of elastin fibres, which gives the skin its flexibility. As individuals age, the bony skeleton and soft tissues of the face lose volume, drop and shrink to produce a wider orbital aperture and less anterior projection (1). This decreases the overall projection of the cheek and diminishes bony support for the overlying soft tissue structures. This aging process results in drooping eyes and tear trough deformity, lateral eyebrow ptosis, malar descent, a heavy jaw line and hypertonic contractions of the depressor muscles (2). Aging is also accompanied by a decline in the activity of the sebaceous glands, thus reducing the skin's ability to retain moisture and maintain suppleness.

Anatomy of the face

Facial anatomy is complex since the three-dimensional aspect of the face must be considered in relation to functional anatomy and volume. All facial anatomical components are in permanent motion and muscle contractions result in facial expression (2). Each layer of the midface has an influence on facial morphology and it is important to assess the extent to which each anatomical component contributes to facial disharmony before selecting the corrective technique of choice (3). The thickness, colour, mobility and texture of facial skin are variable and the fat layer, which is located in the subcutaneous tissue layers between the skin and muscles, also varies in thickness. Many of the signs of aging are due to the loss of subcutaneous fat and so the use of sub-dermal fillers or implantation of autologous fat can help create a more youthful appearance, thereby reducing many of the signs of aging. This is particularly important for the malar fat pad, which lies superficial to the zygomaticus muscles and extends from malar eminence to the

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nasolabial crease (i.e. the sub-ocularis oculi fat, or SOOF) (3–8).

The occurrence of wrinkles due to muscular hyperactivity, such as crow's feet and horizontal forehead wrinkles, can be corrected using botulinum neurotoxin (BoNT) or surgical techniques (2,7,9–13).

Volumetric treatments for facial rejuvenation

Skin resurfacing techniques, such as peeling, laser resurfacing and dermabrasion, as well as use of dermal fillers, can be used to rejuvenate the skin and reduce wrinkles. However, an increase in volume is an important part of facial rejuvenation. It is particularly significant where there is soft tissue loss or inadequate volume, such as treatment of nasolabial folds, hollow eyes or sagging malar areas, which occur due to a reduction of the malar fat pad.

Volumetry can be defined as the science of volume enhancement and focuses on the areas of volume loss, the causes of volume loss, therapeutic methods and assessment and measuring methods (9). Traditional approaches to volumetry have tended to divide the face into the upper face, midface and lower face/neck, and treatments largely comprised skin and superficial and deep plane tightening and replacement (10–16). However, over the past 10 years, there has been a greater focus on the midface region (defined as the area lying between the bicanthal and oral commisural planes) since it is one of the first areas that ages (Figure 1). The introduction of new techniques such as injectable fillers comprising non-permanent gels, such as Surgiderm®, Juvéderm ULTRA® and Voluma®; fat grafting and preservation; endoscopic procedures; and the use of botulinum neurotoxin (BoNT) have all radically changed the nature of facial rejuvenation (2,3).

Dermal fillers are non-surgical cosmetic treatments that are used to give a more youthful appearance by restoring facial volume or fullness. They work by reducing or eliminating lines, wrinkles and folds in the skin. A major advantage of these treatments is that the effect is seen immediately after treatment (2). There are various kinds of safe, natural and synthetic materials used as dermal fillers, including porcine and bovine collagen, calcium hydroxylapatite and hyaluronic acid (HA). With respect to the face, two forms of dermal fillers are generally used: semi-permanent fillers (e.g. Radiesse® or Sculptra®) and non-permanent fillers (e.g. Juvéderm or Restylane®).

Hyaluronic acid

HA is a naturally occurring linear polysaccharide that is a component of all connective tissues, such as in skin, bones, joints and eyes. HA acts as a lubricant and moisturiser due to its hydrophilic properties, allowing it to attract and attach to water molecules. HA dermal fillers can be used in facial rejuvenation since they integrate with the surrounding tissue, allowing free passage of oxygen and hormones. This helps to reduce the signs of aging by moisturizing the skin and returning its elasticity and tone, producing natural, healthy-looking facial skin.

HA fillers are administered on an outpatient basis, usually using local anaesthesia, as a series of tiny injections under the surface of the skin at the sub-dermal and dermal levels. The amount injected depends on the depth and size of the skin defect or wrinkle. A key treatment benefit is that HA dermal fillers require very minimal downtime, allowing patients to return to work and normal daily activities almost immediately after treatment. Over time, HA fillers are broken down by natural biological processes and removed from the body. HA is clinically produced, usually from bacterial rather than from animal or human sources and because of its uniform structure throughout all living species, adverse immune reactions are rare. The versatility of HA products expands the physician's treatment options and its low risk of immune reactions makes HA products the cornerstone of injectable fillers, which are indisputably gaining ground in the search for the ideal implant (9,17,18).

Voluma

Juvéderm Voluma is a new HA sub-dermal facial filler produced through bacterial fermentation of *Streptococccus equi*. It is a smooth consistency gel with a 20 mg/ml total HA concentration typically administered in 2 ml syringes using a 21-gauge needle or an 18 G cannula. Assessment of the physical and chemical components reveal that the composition of Voluma comprises a mix of low and high molecular weight HA. Higher molecular weight products have more repeating units in the polymer chain compared with low molecular weight products, and this influences the composition and cohesivity, which are key elements of volumizing HA fillers. Thus, Voluma shows greater cohesivity and viscosity compared with 100% high molecular weight products (19).

This composition of Voluma makes optimum use of bridges between cross-linking agents using a cross-linking agent called BDDE. This, along with its lower molecular weight, results in a higher crosslink ratio with increased cohesivity and subsequent reduced extrusion and flow (14), thus enabling the gel product to retain its structure following a deep injection. Voluma is designed to be a viscous and robust sub-dermal filler which is easy to inject, with volumes typically ranging from 1 to 3 cc on each side of the face (9). These qualities mean that it has a higher lift capacity, ideally suited

Figure 1. Midfacial anatomy. (A) Anatomical correlations of midface soft tissue and clinical morphological aspect. Note in yellow/orange the convexity of the malar fat pad above the dark red zygomaticus muscle. The nasolabial fold is created by the malar fat pad sliding and the zygomaticus contractions. The facial nerve is vertical oblique, below the superficial temporal artery (it is in fact the frontal branch of the facial nerve). The facial nerve should not be affected by midface Voluma injections, which are lower and more central. Note that in the midface area the branches of the facial nerve are mostly under the zygomaticus muscle (3,4,9,12,13,15). (DAO=depressor anguli ori.) (B) Drawing of a turned-down thick flap composite facelift, including orbicularis muscle, superficial fat (light yellow) and malar fat pad (dark yellow). Note, in a deeper plane, the zygomaticus major and minor muscles. Inserted to the periostium of the malar eminence they represent the deepest plane, above which Voluma injections should always stay. The green arrow shows the vector of the horizontal tunnels where Voluma is injected (into and below the SOOF). Part of panel B (the composite facelift flap schema) was provided courtesy of Sam Hamra (ref. 16)

for the correction of deeper wrinkles and folds, as well as for facial volumizing and contouring applications. However, it should not be used for the lips or intradermally. Its effects are fully reversible and resorbable (19).

The objective of this retrospective case analysis was to assess the effectiveness of Voluma HA injectable sub-dermal filler in maintaining increased volume for up to 18 months post-treatment and also to assess its safety.

Materials and methods

Patient selection

Male and female patients attending the clinic between January 2006 and December 2007 who were considered suitable for volumizing treatment were selected for study participation. All patients provided written informed consent prior to participation in any study-specific procedures. Key inclusion criteria comprised patients presenting with hollow sub-palpebral grooves, malar descent, flat cheekbones, hollow temporal areas, scar depression or chin retrusion. Retrospective analysis was made of a total of 102 patient records.

All patients were assessed at baseline according to a four-point volume loss scale comprising 1=normal, 2=evidence of early soft tissue ptosis or atrophy slightly visible, 3=visible depression or descent and 4=severe depression or atrophy.

Local anaesthesia

Voluma was commonly administered under local anaesthesia using lidocaine 2% plus epinephrine, the latter causing vasoconstriction and thereby reducing the risk of bleeding. Anaesthesia has been shown to make the injection of Voluma easier and less traumatic, and it reduces morbidity, specifically bleeding and the risk of haematoma (10,14).

Topical anaesthesia (lidocaine cream) was administered 20 minutes prior to local anaesthesia to reduce needle pain; 1 cc of local anaesthesia was then administered to the midface region using 2-cc syringes via 26- or 30-gauge needles. Troncular anaesthetic block was used to reduce the amount of fluid necessary to obtain the maximum numbed area and also allow the injector to easily assess the quantity of Voluma required, as well as reduce post-treatment swelling. Voluma was administered under combined percutaneous and local anaesthesia in 67 patients (65.7%), local anaesthesia was used alone in 38 patients (37.3%), percutaneous anaesthesia was used alone in five patients (4.9%) and there were two patients (1.9%) who received no anaesthesia.

Dosing and injection technique

Patients received doses of Voluma to the midface region according to their baseline volume loss score. Those patients with a score of 2 were administered 1

cc per side, those with a score of 3 received 2 cc per side/area, and those with a score of 4 required 3 cc per side/area, plus an additional touch up using 2 cc per area. Patients were mostly (92%) injected into the midface, which comprised the sub-malar/sub-palpebral area (central midface) and malar area (lateral midface).

Voluma was administered via a 19-gauge cannula in 28 patients (27.5%) and by a 21-gauge needle in 74 patients (72.5%). The injection technique commenced with horizontal injections following a line from the most prominent edge of the malar bone forward towards the nose and strictly inferior to the orbital rim (see green arrow on Figure 1). The injection depth level was under the orbicularis muscle, under or into the malar fat pad and under or into the SOOF, but never sub-periosteal (7,12). The piston of the Voluma syringe was continuously pushed during the procedure to avoid damaging deep facial components and, in so doing, multiple tunnels were created. The small bolus of viscous HA is thick and always precedes the tip of the needle, thereby acting as a cushion to gently dissect the tissue before the needle. In our experience, Voluma treatment is best administered by crossing the various tunnels in different planes to allow the product to spread into and under the fat pads. It is important to avoid any large boluses.

For more effective filling, a second vector can be used for midface injections, which creates a vertical oblique line of injection. The injection line goes from a point at the top of the nasolabial fold, 2 mm down to the nostril junction and up to the malar eminence. If the sub-palpebral (central midface) area also needs filling, injections are performed upwards, in a fan-shaped pattern to recreate the SOOF and the malar fat pad. However, it is imperative to stop under the orbital rim (one trick is to use the index finger to palpate the orbital rim and so protect the orbits from accidental injection). The injection level is very deep, under or into the fat pad, but always above the zygomaticus muscles. In this area it is important to know the position of the sensitive infra-orbital nerve (coming out of a notch through the maxilla bone, 2 cm under the orbital rim, below the elevator nasi and labialis muscles) (3–5) (Figure 2).

When massage is performed at the end of the injection procedure, Voluma spreads gently into all the tunnels, resulting in a harmonious, natural look.

Assessments

All patients were assessed at 1 month and again at 6–18 months post-injection by the principal investigator using the Global Aesthetic Improvement Scale (GAIS). This comprised a five-point scale, where 1=very much improved, 2=much improved, 3=improved, 4=no change and 5=worse. In addition, investigator assessment of reduction in volume loss was assessed at 1 month and at 6–18 months post-injection.

Patients were asked to provide an assessment of efficacy at 6–18 months post-injection using a five-point scale, where 1=very good, 2=good, 3=not very good, 4=quite bad and 5=very bad. Patients were also asked to complete a study-specific questionnaire that asked if they would recommend the treatment to others, whether they felt the treatment resulted in benefits, and whether treatment resulted in patients feeling 'more attractive', 'better' and 'more confident'.

Statistical analysis

Data were analysed using descriptive statistical techniques (i.e. categorical data were presented

Figure 2. Injection tunnels for Voluma application. Arrows represent vectors of Voluma injections. Note the crossing of the vectors/tunnels that allows a harmonious injection in a tridimensional way to create a new convex volume. It also reduces the height of the lower eyelid to give a fuller, younger, more attractive and healthy look to the midface area (1,3,20).

using frequency distribution tables, continuous data by summary statistics: N, mean, standard deviation, median, Q1, Q3, minimum, maximum). All analyses were of a purely exploratory nature.

Results

Demographic and baseline characteristics

A total of 102 patient records were reviewed retrospectively, comprising 93 females (91%) and nine males (9%), with a mean age of 51.3 years (range: 26–80 years). Prior to Voluma injection, the majority of patients (98%) were noted to have stage 2 or 3 volume loss according to the volume loss scale (2=evidence of early soft tissue ptosis or atrophy slightly visible, 3=visible depression or descent). Sixty-five patients (64%) had previously undergone treatment with other dermal fillers and 48 patients (47%) had received prior BoNT (Vistabel) treatment.

Dosing

Patients received treatment with Voluma injectable sub-dermal filler in one session on each midface side for facial augmentation primarily for correction of hollow sub-palpebral grooves, malar descent or flat cheekbones. The total mean dose injected in the midface was 2.8 cc (range 1–6 cc). A few cases of hollow temporal areas, scar depression or chin retrusion were injected at a mean dose of 1.9 cc (range 1.2–2cc). The most commonly injected sites were the combined malar and sub-palpebral regions (51%) and the sub-palpebral region (22%) (Table I) (note the midface zone [sub-palpebral plus malar] was treated in 94 cases [92%]). The mean duration of patient follow-up was 50.4 weeks (range: 1–81 weeks).

Investigator assessment of aesthetic results

Results from the investigator assessment of GAIS at 1 month post-treatment showed that the majority of patients were 'very much improved' (73 patients [72%]) or 'much improved' (27 patients [26%]). Only one patient was rated as 'improved' and one patient was rated as 'no change' (both 1%). No patient was considered 'worse' following Voluma treatment (Table II). Investigator GAIS assessment at 6–18 months post-treatment revealed that 65 patients (64%) were still considered as 'very much improved', 17 patients (17%) were rated as 'much improved' and 18 patients (18%) were considered 'improved'. Only one patient (1%) was judged as 'no change' and no patient was considered 'worse' at this time point (Table II).

Table I. Injected sites.

Region	Number of patients (%)
Malar and sub-palpebral	52 (50.98)
Sub-palpebral	22 (21.57)
Malar	13 (12.75)
Other (nasolabial folds, cheek, temple, eyebrow, chin, nose)	8 (7.84)
Malar, sub-palpebral and other (cheek, chin)	3 (2.94)
Malar and other (cheek, chin)	2 (1.96)
Sub-palpebral and other (cheek, chin)	2 (1.96)

Table II. Results of GAIS (1 month and 6–18 months post-treatment).

GAIS	Categories	1 month post-treatment *n* (%)	6–18 months post-treatment *n* (%)
1	Very much improved	73 (71.6)	65 (64.4)
2	Much improved	27 (26.5)	17 (16.8)
3	Improved	1 (0.9)	18 (17.8)
4	No change	1 (0.9)	1 (0.9)
5	Worse	0 (0)	0 (0)

Investigator assessment of volume restoration

Investigator assessment of the reduction in volume loss at 1 month revealed that 89 patients (87%) were stage 1 (normal) and 13 patients (13%) were stage 2 (evidence of early soft tissue ptosis or atrophy slightly visible). A comparison of volume loss at baseline versus the assessed reduction of volume loss after the first Voluma injection showed 64 patients (63%) changing from stage 2 at baseline to stage 1 following the first treatment, 24 patients (24%) changing from stage 3 to stage 1, 10 patients (10%) changing from stage 3 to stage 2, one patient (1%) changing from stage 4 to stage 1 and one patient (1%) changing from stage 4 to stage 2 (Table III). By 6–18 months post-treatment, the majority of patients were still considered to be stage 1 (63 patients [62%]), or stage 2 (31 patients [30%]), with only four patients (4%) judged to be stage 3 and 2 patients (2%) were judged stage 4.

Investigator assessment of the overall volumizing effect was judged to be 'very good' in 83 patients (81%), 'good' in 12 patients (12%), 'moderate' in three patients (3%) and 'bad' in two patients (2%) (Table IV).

Patient assessment of aesthetic result

Patient assessment of treatment efficacy at 6–18 months showed that all patients considered Voluma to be either 'very good' (71 patients [70%]) or 'good' (29 patients [28%]). Similarly, results of the patient questionnaire clearly revealed that the vast majority of patients would recommend Voluma treatment to others since it provided benefits, with patients indicating that they felt more attractive, with better self-esteem and greater confidence (Figure 3).

Table III. Quantification of pretreatment volume loss and staging following first treatment.

Baseline staging		Staging following first treatment			
	Overall at baseline	I	II	III	IV
I	**0**	0	0	0	0
II	**66 (64.71)**	64 (62.75)	2 (1.96)	0	0
III	**34 (33.33)**	24 (23.53)	10 (9.80)	0	0
IV	**2 (1.96)**	1 (0.98)	1 (0.98)	0	0
Overall at first treatment		**89 (87.25)**	**13 (12.74)**	**0**	**0**

Data presented as number of patients (%). I=normal; II=evidence of early soft tissue ptosis or atrophy slightly visible; III=visible depression or descent; IV=severe depression or atrophy.

Table IV. Overall investigator assessment of volumizing effect.

Stage	Category	Number of patients (%)
1	Very good	81 (81)
2	Good	12 (12)
3	Moderate	3 (3)
4	Bad	2 (2)
5	Very bad	0 (0)

Additional Voluma treatment was required in 16 of the 102 patients (16%), with the main reasons being treatment refinement, a need to increase the volume in the injected area, presence of a slight facial asymmetry or to provide eyebrow lift (by augmenting eyebrow volume and projection).

Adverse events

Treatment was well-tolerated, with only nine temporary adverse events recorded in eight patients (8%). The adverse events lasted between 3 and 42 days. The reported adverse events were swelling (one case), haematoma (three cases), overcorrection (four cases) and hypersensitivity (one case). The adverse events considered to be 'likely', 'possibly' or 'certainly' due to Voluma treatment comprised swelling, overcorrection and hypersensitivity, while the three cases of haematoma were considered 'unrelated' to Voluma treatment but related to the mechanical injection process. Treatment, in the form of oral anti-inflammatory medication and oedema reduction with Extranase®, was required in one patient suffering severe haematoma of the left midface which lasted 21 days. No other patients required treatment for their adverse events and seven patients made a full recovery (data missing for one patient).

Discussion

An attractive face is characterized by smooth, round contours, high cheekbones, oblique, hollow jowls and a thin, well-defined jawline. These features together comprise the 'triangle of beauty' or 'heart of face', with its base at the top and summit below (20) (Figure 4). This 'triangle of beauty' or 'heart of face' evokes feelings of desire and attraction, while, in contrast, older or unattractive individuals are found to have the reverse triangle or heart, where the summit is at the top and the base is below. Here, the

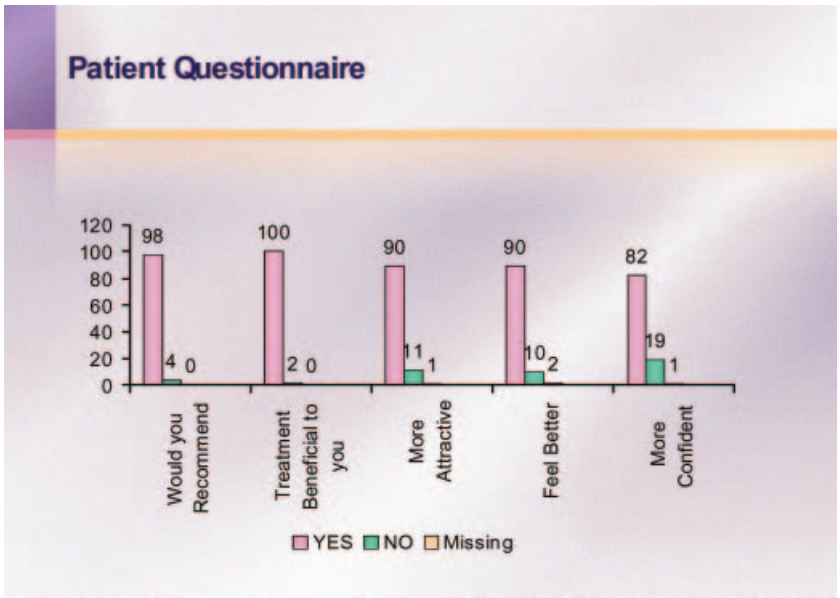

Figure 3. Results of patient questionnaire.

Figure 4. Triangle of beauty or heart of face. A 57-year-old woman treated with Voluma, BOTOX and Juvéderm Ultra. (A) Before treatment: this shows a reverse heart that is considered less attractive. (B) At 3 months after treatment, with a more attractive face showing a 'heart of beauty'. The same woman before (C) and 12 months after (D) treatment. Voluma: 1 cc per side in midface for slight atrophy (scale 2); BOTOX: upper and lower face (repeated every 5 months) and orbicularis oculi muscles 10 U/side, glabella 25 U, platysma 10 U/side; Juvéderm Ultra 3: 0.4 cc per side for nasolabial folds, 0.4 cc to upper lip. (E) Before treatment and (F) 12 months after.

face is characterized by features such as drooping eyes, tear trough deformity, lateral eyebrow ptosis, malar descent, a hollow sub-orbicularis area, a large, heavy jawline and hypertonic depressor muscle

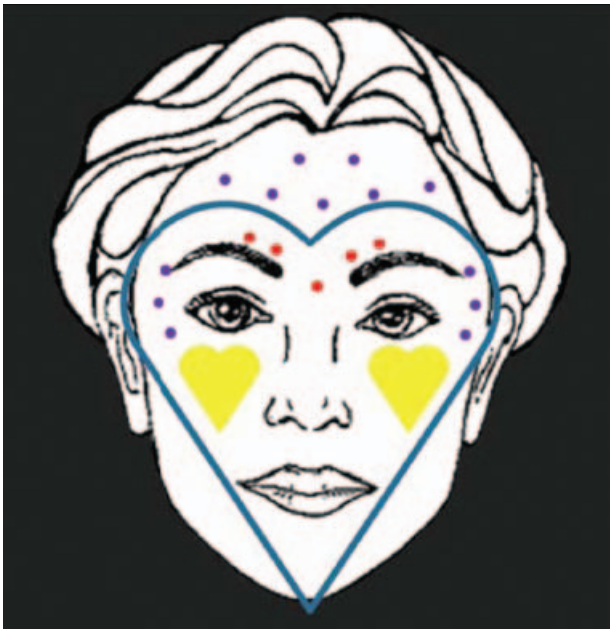

Figure 5. Typical BoNT and filler injection facial sites. BoNT injection sites: purple dots=2–4 U, red dots=4 U; Voluma injection sites: yellow areas.

contractions that pull down the soft facial components (2,3,20).

The aging process is caused by a combination of factors and results in both dynamic and volumetric changes. The aim of midface enhancement is to recreate malar volumes, smooth nasolabial folds, reposition lateral canthi, fill the lower eyelid concavities, correct crow's feet and lift the eyebrows to produce improved facial muscle balance, giving a natural result.

Successful facial rejuvenation can best be achieved by detailed knowledge of facial anatomy and a clear understanding of both dynamic and volumetric anatomical changes (3,13,20). Dynamic changes arise from contraction of the facial musculature and modification of the action of the muscles of expression can be achieved with BoNT, which results in relaxation of muscle tonicity and contraction and a smooth face (21).

Volumetric changes are caused by tissue ptosis and/or atrophy and are most commonly seen in the mid and lower face. Volumetric changes can be addressed either surgically or non-surgically, depending on the diagnosis. Where there is adequate volume but a desire for re-shaping, facial remodelling can be achieved using facelift or blepharoplasty (3,9,10,14,22).

In cases where there is soft tissue loss, inadequate volume or the presence of wrinkles, surgical intervention, such as fat grafting, and non-surgical techniques, such as use of injectable sub-dermal fillers, are now very popular, particularly with the emergence of new volumetric agents such as Voluma.

All medical procedures have associated risks and, in general, the more invasive the procedure, the

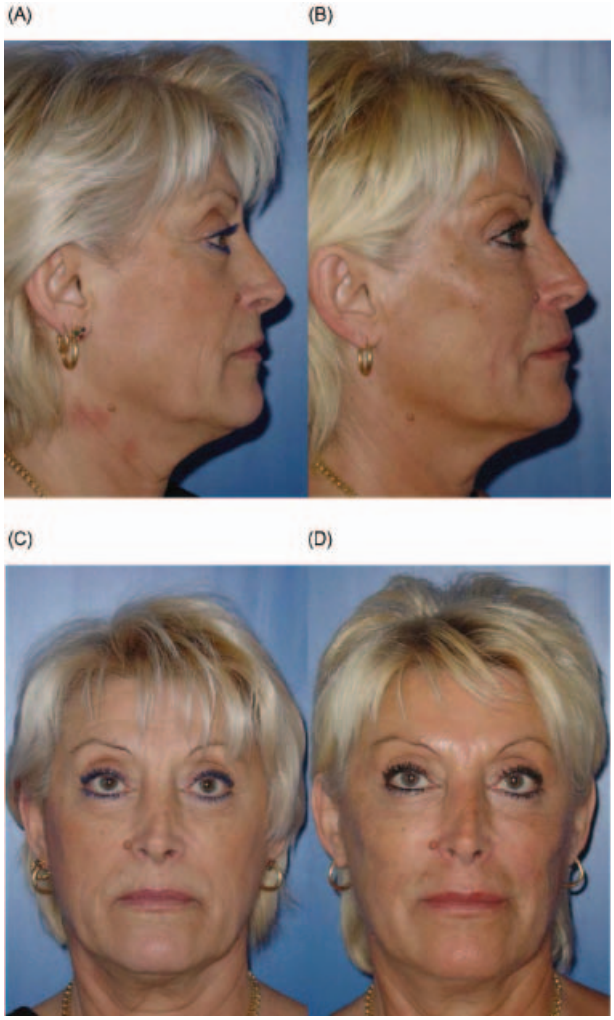

Figure 6. Results of Voluma treatment. A 52-year-old lady before (A) and after (B) Voluma, Juvéderm Ultra and BOTOX treatment. Voluma: 2 cc per side in midface for malar descent and mild fat atrophy (scale 3); BOTOX: upper and lower face (repeated every 5 months), orbicularis oculi muscles 10 U/side, glabella 20 U; Juvéderm Ultra: 0.8 cc per side for nasolabial folds and jowl wrinkles, 0.8 cc to upper and lower lip. (C) Before treatment with Voluma; (D) 6 months after treatment, with a more convex midface.

greater the associated risk. Patients who undergo facial rejuvenation may experience some temporary adverse effects, such as mild redness, swelling, chemosis, bruising and minor discomfort, while scarring, persistent redness, or permanent pigment changes may occur as a result of more invasive procedures. Non-surgical treatments, such as the use of injectable dermal fillers, differ from their surgical alternatives by rejuvenating the skin to reverse the visible effects of aging, rather than invasive, surgical intervention that manipulates the skin in its existing aged condition. Facial plastic surgery also improves all facial components by replacing or recreating volume lost through fat or muscle degeneration. Skin rejuvenation improves the quality of the skin by increasing the production of elastin and collagen and restoring the moisture content of the skin.

This retrospective case analysis indicates that Voluma injectable HA sub-dermal facial filler treatment results in clear aesthetic improvements, comprising a pleasing attractive midface area that resulted in increased self-esteem and greater confidence in the majority of patients, according to both the investigator and patient assessment, for up to 18 months post-treatment. Its beneficial effects are achieved due to the fact that the chemical composition of Voluma is high viscosity and high cohesivity. With a total of 99% of patients considered 'very much improved', 'much improved' or 'improved' according to investigator GAIS assessment at 6–18 months, these results concur with other studies that demonstrate the benefits of HA fillers compared with other facial fillers, such as bovine collagen and autologous fat (23–26). Voluma is particularly suitable for the treatment of malar areas and/or hollow grooves under the eyes, known as the sub-palpebral area. It may also be used successfully in the chin region and for the treatment of scar depression.

Investigator assessment of volume loss confirmed that most patients were judged to be either stage 1 (normal) or 2 (evidence of early soft tissue ptosis or atrophy slightly visible) 1 month after treatment, which was maintained at 6–18 months post-treatment. Patient assessment of efficacy was either 'very good' or 'good' in all cases, with patients confirming that they would recommend treatment to others since it provided benefits in the form of increased attractiveness and improved self-esteem.

The safety profile of the treatment was good, with only 8% of patients experiencing adverse events, the majority of which were resolved without any additional intervention being required. One case of swelling and one case of hypersensitivity were reported as 'likely', 'possibly' or 'certainly' due to Voluma treatment, but generally the rate of such reactions was low, probably due to the non-animal origin of the HA in Voluma reducing the risk of development of an immunological response to xenogeneic protein. No cases of infection following treatment were reported. Furthermore, no cases of migration were seen following Voluma treatment, even though such effects have been reported with other products such as Restylane Sub-Q (27,28).

Injectable agents for soft tissue augmentation have been widely available for more than 20 years, but new interest in them has emerged with the introduction of BoNT. Whilst dynamic changes to smooth and reshape the upper, mid and lower face can be modified with products such as BoNT, an increase in volume is also an important part of facial rejuvenation. Combination therapy, such as BoNT and HA facial fillers, both of which individually have predictable aesthetic results and can be administered in the office setting, can be used together in customized proportions to meet individual patient needs and can provide each patient with the best possible treatment outcome to achieve maximum

aesthetic results (29). Furthermore, combined BoNT and HA treatment can enhance the benefits by as much as 50%, leading to further optimized results and greater patient satisfaction (30) (Figures 5 and 6).

In conclusion, detailed anatomical expertise combined with the use of the latest techniques (i.e. combining BoNT with sub-dermal fillers such as Voluma), are paramount in effecting volumetric and dynamic facial modifications, to achieve a natural, harmonious, non-surgical approach to facial rejuvenation and a recreation of the desired 'triangle of beauty' (20). This retrospective review of clinical experience in more than 100 patients demonstrates interesting initial results, but further methodologically rigorous studies comprising large, long-term, prospective, randomized clinical trials in the cosmetic field are required to establish the performance of Voluma subdermal filler alone and in combination with BoNT, and both patient and investigator acceptability of treatment over longer periods of follow-up.

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References

1. Finn JC, Cox SE, Earl ML. Social implications of hyperfunctional facial lines. Dermatol Surg. 2003;29:450–5.
2. Raspaldo H. Facial design, architecture and volume – the new 3D sculpture using botulinum toxin deep injectable fillers: Facial rejuvenation using Btx expertise combined with injectable fillers in upper, mid and lower face. Allergan Academy, London, 13 April 2007; poster session.
3. Raspaldo H, Bettens RMA, Giordano P. Midface enhancement. In: Vuyk HD, Lohuis PJ, editors. Facial plastic and reconstructive surgery. London: Hodder Arnold; 2006. p. 101–22.
4. Belhaouari L, Gassia V. L'Art de la toxine botulique en esthétique [in French]. Paris: Arnette Blackwell (now part of Wolters Kluwer Company); 2006.
5. Saban Y, Polselli R, Santini J, Raspaldo H, Lagier J. Atlas of surgical anatomy of the face and neck. Masson: Paris; 1994.
6. Ramirez O. The SOOF lift: Its role in correcting midfacial and lower facial asymmetry in patients with partial facial palsy. Arch Facial Plast Surg. 2003;5:449.
7. Tessier P. Le lifting facial sous-périosté [in French]. Ann Chir Plast Esthet. 1989;34:193–7.
8. Hamra ST. Suborbicularis oculi fat pads. Plast Reconstr Surg. 1996;97:484–6.
9. Raspaldo H. Lifting vidéo-assisté: Évolution (video-assisted endoscopic lifting: Development) [in French]. Rev Laryngol Otol Rhinol (Bord). 1997;118:57–64.
10. Raspaldo H, Toma A. Endoscopic face lift. 4th European Congress of Oto-Rhino-Laryngology, Head and Neck Surgery, Berlin, Germany, 13–18 May 2000. Bologna: Medimond SRL; 2000. p. 483–92.
11. Botti G (editor). Chirurgia estetica dell'invecchiamento facciale [in Italian]. Padova: Piccin spa; 1995. p. 4.
12. Raspaldo H, Santini J, Carlotti B. Mask-lift et liftings profonds composites: Dangers du nerf facial et leurs solutions [in French]. Rev Chir Esthet Langue Fr. 1993;72:19–33.
13. Raspaldo H. Lifting harmonieux (Harmonious Rhytidectomy): Technique-philosophie [in French]. JFORL (Journal français d'oto-rhino-laryngologie, audiophonologie et chirurgie maxillo-faciale). 1996;45:254–67.
14. Ascher B. Volumetric rejuvenation: A preliminary study. In: Azaïs V, Bernard S, Chaudron C, Villain F, editors. Surgiderm Actualités 3. Paris: A CORNEAL development publication; 2006. p. 5–7 (www.surgiderm.com – aesthetic@corneal.com).
15. Santini J, Raspaldo H, Kestemont P, Magnani M. Surgical planes of dissection of the face: Anatomic basis for composite face lifts. In: FACE (Facial Aesthetic Communication in Europe); 1994.
16. Hamra S. Composite rhytidectomy. Plast Reconstr Surg. 1992;90:1–13.
17. Lupo MP. Hyaluronic acid fillers in facial rejuvenation. Semin Cutan Med Surg. 2006;25:122–6.
18. Carruthers A, Carruthers J. Non-animal-based hyaluronic acid fillers: Scientific and technical considerations. Plast Reconstr Surg. 2007;120(6 suppl):33S–40S.
19. Tezel A, Introduction and overview of volumizing and contouring product features and benefits. Irvine, CA: Facial Executive Council, Allergan Inc (data on file).
20. Fagien S, Raspaldo H. Facial rejuvenation with botulinum neurotoxin: An anatomical and experiential perspective. J Cosmet Laser Ther. 2007;9(suppl 1):23–31.
21. Carruthers J, Fagien S, Matarasso SL, the Botox Consensus Group, Consensus recommendations on the use of botulinum toxin type A in facial aesthetics. Plast Reconstr Surg. 2004;114(6 suppl):1S–22S.
22. Fagien S. Botulinum toxin type A for facial aesthetic enhancement: Role in facial shaping. Plast Reconstr Surg. 2003;112(5 suppl):6S–18S; Discussion, 19S–20S.
23. Lupo MP, Smith SR, Thomas JA, Murphy DK, Beddingfield FC 3rd. Effectiveness of Juvéderm Ultra Plus dermal filler in the treatment of severe nasolabial folds. Plast Reconstr Surg. 2008;121:289–97.
24. Baumann LS, Shamban AT, Lupo MP, Monheit GD, Thomas JA, Murphy DK, et al. Comparison of smooth-gel hyaluronic acid dermal fillers with cross-linked bovine collagen: A multicenter, double-masked, randomized, within-subject study. Dermatol Surg. 2007;33(suppl 2):S128–35.
25. Kanchwala SK, Holloway L, Bucky LP. Reliable soft tissue augmentation: A clinical comparison of injectable soft-tissue fillers for facial-volume augmentation. Ann Plast Surg. 2005;55:30–5.
26. Lindqvist C, Tveten S, Bondevik BE, Fagrell D. A randomized, evaluator-blind, multicenter comparison of the efficacy and tolerability of Perlane versus Zyplast in the correction of nasolabial folds. Plast Reconstr Surg. 2005;115:282–9.
27. DeLorenzi C, Weinberg M, Solish N, Swift A. Multicenter study of the efficacy and safety of subcutaneous non-animal-stabilized hyaluronic acid in aesthetic facial contouring: Interim report. Dermatol Surg. 2006;32:205–11.
28. Lowe NJ, Grover R. Injectable hyaluronic acid implant for malar and mental enhancement. Dermatol Surg. 2006;32:881–5.
29. Klein AW, Fagien S. Hyaluronic acid fillers and botulinum toxin type a: rationale for their individual and combined use for injectable facial rejuvenation. Plast Reconstr Surg. 2007;120(6 suppl):81S–8.
30. 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(6 suppl):41S–54S.